
From: Jambou, Robert (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=JAMBOUR]
Sent: 7/7/2016 4:47:25 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]; Carr, Sarah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=CARRS]; Dodson, Sara (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Dodsonse]; Volkov, Marina (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=nimh/cn=mvolkov]; Fennington, Kelly (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=FENNINGTONKNEW]
Subject: FOIA Request - 45260_Goldman re: Union for Affordable Cancer Treatment (UACT)
Attachments: 45260_Incmg.pdf

Hi all,

Please see the attached request. I am notifying you of a FOAI request received today 7/7/2016.
The requester is Andrew Goldman, Counsel for Knowledge Ecology International.
The scope of the response is January 14, 2016 through July 7, 2016 (the date the net is cast).

Please do not delete any e-mails or other records responsive to this request.
Please begin your search ASAP as this request was received by NIH on June 29, 2016 and ideally should be completed within 20 working days.

When you are ready to provide responsive records, please notify me that I can assist in making this as efficient as possible.

Thanks to all...

Bob J.

GOLDMAN

DATE: 7/7/2016

TO: **ROBERT JAMBOU**
OBA FOIA Coordinator
Building Rockledge Center I, Rm.
733
6705 Rockledge Dr - Suite 750
Bethesda, MD 20817

FROM: NIH FOIA Office, OD/OCPL

SUBJECT: FOIA Case No. 45260 - FOIA Log No. 2016/437

The attached FOIA request is forwarded to you for the following action:

FOR DIRECT REPLY. Enter the case into the FOIA Tracking System. Upon completion, please forward a complete Close-Out package to the NIH FOIA Office.

If you forward this request to a program office within your IC, keep a copy of this request in your FOIA Case file. As the IC FOIA Coordinator, you are responsible for the collection of records and follow-up until the request is closed.

Please contact the NIH FOIA Office on 301-496-5633 or at [nihfoia@mail.nih.gov](mailto:.nihfoia@mail.nih.gov) if you have any questions.

COMMENTS: Bob, I've already entered this request into the tracking system, but please answer the requester directly.

Redmond, Tim (NIH/OD) [E]

From: Andrew S. Goldman <andrew.goldman@keionline.org>
Sent: Wednesday, June 29, 2016 2:34 PM
To: NIH FOIA
Cc: Claire Cassedy; Hammersla, Ann (NIH/OD) [E]
Subject: FOIA Request re Xtandi
Attachments: nih-foia-request-06-29-2016-Xtandi (1).pdf



To Whom it May Concern:

Request for Documents Under FOIA

Under the Freedom of Information Act, Knowledge Ecology International (KEI) requests all documents, correspondence, and notes from the National Institutes of Health (NIH) regarding the petition submitted by KEI and the Union for Affordable Cancer Treatment (UACT) in January 2016 that requested that the NIH use its rights in patents under the Bayh Dole Act for the prostate cancer drug enzalutamide, marketed in the U.S. by Astellas Pharma as Xtandi.

Specifically, KEI requests all documents, correspondence, and notes that were generated internally or may have been submitted or sent to any NIH office, regarding the above petition, by: other offices, institutes, or components of the NIH; the United States Department of Health and Human Services and any other federal departments or agencies; or non-governmental persons or entities.

In the scope of this particular FOIA request, non-government person or entity includes, but is not limited to, pharmaceutical companies, corporations, industry associations, civil society organizations, non-profit organizations, consultants, or private citizens.

The period of this request is from January 14, 2016 to the present.

Fee Waiver Request

As a non-profit organization, KEI requests a waiver of fees, on the grounds that the information will be disseminated broadly, is not related to a commercial use, and will deepen public understanding of government decisionmaking, policy priorities, and informational transparency.

KEI itself has published or been quoted widely as regards issues concerning government management of intellectual property as it relates to public interest, consumer interest, and public health. James Love, Director of KEI has personally written on these issues in publications such as the Financial Times and in several academic and policy journals.

The stories below demonstrate that in the past, KEI has effectively used FOIA requests to widely disseminate information that is in the public interest, and we can provide many others to support our fee waiver request.

- Kimberly Kindy, Filmmakers' group tries to reshape treaty that would benefit the blind, Washington Post, web version, June 22, 2013, print version June 23, 2013.
- Paige McClanahan, US film industry tries to weaken copyright treaty for blind people: Treaty to make copyrighted works available for visually impaired people – 90% of whom live in global south – coming up against film lobby. The Guardian, Monday 24 June 2013.

- Mike Masnick, MPAA's Actions, Emails Show That They're Doing Everything Possible To Screw Over The Blind: from the how-can-they-deny-it? dept, TechDirt.Com June 24, 2013.
- Catherine Saez, WIPO Negotiators Reach Breakthrough On "3-Step Test" In Treaty For Blind, IP-Watch.Org, Published on 24 June 2013.
- Timothy Lee, Emails show cozy relationship between Obama trade negotiators and industry groups, Washington Post, web version, November 29, 2013.

We are happy to provide more information to support our request for a waiver of FOIA fees and to clarify the terms of this request if needed. If possible, please provide the FOIA response via electronic copy.

Thank you for your assistance.

Sincerely,

Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

From: Niebylski, Charles (NIH/NIDDK) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=NIEBYLSKICD]
Sent: 10/25/2016 3:13:22 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Fine, Amanda (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Fineab]; Payne, January (NIH/NIDDK) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Paynejw0ac]
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

b5

From: "Niebylski, Charles (NIH/NIDDK) [E]" <niebylskicd@niddk.nih.gov>
Date: Tuesday, October 25, 2016 at 11:11 AM
To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>
Cc: "Fine, Amanda (NIH/OD) [E]" <amanda.fine@nih.gov>, "Payne, January (NIH/NIDDK) [E]" <january.payne@nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

Mark:

My comments below

-- My questions would basically be:

(1) How do you respond to their complaint
[about drug pricing]?

(2) What are the institute's priorities when
licensing these drugs?

(3) How much progress has this licensee made
on marketing this drug?

(4) What were the results of the Phase 1 trial
that NIH funded on this drug?

(5) Some observers are asking: why grant
an exclusive license to a small, unknown
company with no track record of bringing
drugs to market?

b5

PS - I note that the NIH's response to KEI's FOIA request on this matter (referred to below) does not appear to have been posted on the KEI website yet.

Hope this helps,
Chuck

Charles Niebylski, PhD JD

Director

Technology Advancement Office (TAO)

National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)

National Institutes of Health

Department of Health & Human Services

Building 12A, Room 3011

Bethesda, MD 20817-5632

Ph: 301-435-8146

nibs@nih.gov

From: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>
Date: Monday, October 24, 2016 at 4:49 PM
To: "Niebylski, Charles (NIH/NIDDK) [E]" <niebylskicd@niddk.nih.gov>
Cc: "Fine, Amanda (NIH/OD) [E]" <amanda.fine@nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

Chuck:

See thread below. Could you help answer the questions about NIH licensing?

Thanks
Mark

Sent from my iPhone

Begin forwarded message:

From: "Portilla, Lili (NIH/NCATS) [E]" <portilll@mail.nih.gov>
Date: October 24, 2016 at 9:22:01 PM GMT+1
To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>, "Vepa, Sury (NIH/NCATS) [E]" <sury.vepa@nih.gov>
Subject: RE: Interview request/chlorcyclizine pricing: BuzzFeed News

REL0000024069

Mark:

b5

Regards,

Lili

*Lili M. Portilla, MPA
Director, Office of Strategic Alliances
National Center for Advancing Translational Sciences, NIH
9800 Medical Center Drive, Room 3042
Rockville, MD 20850
Phone: 301-217-2589
Email: Lilip@nih.gov*

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 24, 2016 3:51 PM
To: Driscoll, Claire (NIH/NHGRI) [E] <cdriscol@mail.nih.gov>; Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

Sorry Claire, meant to copy Lili

Sent from my iPhone

On Oct 24, 2016, at 8:50 PM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV> wrote:

b5

Sent from my iPhone

Begin forwarded message:

From: "Fine, Amanda (NIH/OD) [E]" <amanda.fine@nih.gov>
Date: October 24, 2016 at 8:27:59 PM GMT+1
To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>
Cc: "McBurney, Margaret (NIH/OD) [E]"

REL0000024069

<mmcburney@od.nih.gov>, "Hardesty, Rebecca
(NIH/OD) [C]" <rebecca.hardesty@nih.gov>,
"Myles, Renate (NIH/OD) [E]"
<mylesr@od.nih.gov>, "Wojtowicz, Emma
(NIH/OD) [E]" <emma.wojtowicz@nih.gov>
**Subject: RE: Interview request/chlorcyclizine
pricing: BuzzFeed News**

b5

Ideally we'd want a response that is able to answer all
of Dan's questions:

What are the institute's priorities when licensing these
drugs?
How much progress has this licensee made on
marketing this drug?
What were the results of the Phase 1 trial that NIH
funded on this drug?
Some observers are asking: why grant an exclusive
license to a small, unknown company with no track
record of bringing drugs to market?

Thanks Mark! Hope you're not working while on
vacation.

Amanda

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 24, 2016 3:22 PM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Cc: McBurney, Margaret (NIH/OD) [E]
<mmcburney@od.nih.gov>; Hardesty, Rebecca
(NIH/OD) [C] <rebecca.hardesty@nih.gov>; Myles,
Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Wojtowicz,
Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing:
BuzzFeed News

I am available.

b5

b5

Sent from my iPhone

REL0000024069

On Oct 24, 2016, at 8:10 PM, Fine, Amanda
(NIH/OD) [E] <amanda.fine@nih.gov> wrote:

Greetings-

I'm including all three of you per Mark's
out of office and given that the
reporter's deadline is October 28.

NIDDK received the below inquiry from
Dan Vergano at Buzzfeed regarding
Knowledge Ecology International's (KEI)
questions about the drug chlorcyclizine
which had/has a small trial at the CC.
Attached is a back and forth with
NIDDK/NCATS that KEI got through
FOIA. Dan's questions are below. **b5**

b5

Thank you in advance for your input
and guidance,
Amanda

Amanda Fine
Deputy, News Media Branch
National Institutes of Health
Tel: 301-496-7246
Email: amanda.fine@nih.gov
Web: <http://www.nih.gov>

REL0000024069

From: Payne, January (NIH/NIDDK) [E]
Sent: Monday, October 24, 2016 2:54 PM
To: OCPLPressTeam
<OCPLPressTeam@od.nih.gov>;
ODOCPL Interviews (NIH/OD OCPL)
<ODOCPLInterviews@mail.nih.gov>
Cc: NIDDK NIDDKMEDIA (NIH/NIDDK)
<niddkmedia@niddk.nih.gov>
Subject: Interview
request/chlorcyclizine pricing: BuzzFeed News

Hello, NIDDK received an interview request from a BuzzFeed reporter asking about NIH involvement in licensing and drug pricing for chlorcyclizine. Chuck Niebyski, director of NIDDK's Technology Advancement Office, asked that I refer this request to NIH OD as it involves NIH's policy on drug pricing.

Below is the complete email exchange I've had with the reporter, Dan Vergano, and attached is a PDF of an email chain between NIH employees that the reporter received via a public interest group called Knowledge Ecology International, which obtained the records via a FOIA request. (Please note, for background: KEI also published this 2015 post about the same drug.)

Is NIH OD able to respond to this request?

Thank you,
January W. Payne
Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases
NATIONAL INSTITUTES OF HEALTH
Direct 301-435-8115
Cell b6
Office 301-496-3583
www.niddk.nih.gov

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From: Dan Vergano
[mailto:dan.vergano@buzzfeed.com]
Sent: Monday, October 24, 2016 12:29 PM
To: Payne, January (NIH/NIDDK) [E]
<january.payne@nih.gov>
Subject: Re: BuzzFeed News: press
contact / licensing

January,

Thanks for getting back to me

-- The drug is chlorcyclizine (link to license annct below), and the public interest group, Knowledge Ecology International (which often looks at NIH licenses) is complaining that its request for "reasonable pricing" requirements in the license were brushed aside to the detriment of taxpayers. The group has just received a public records request (a portion is attached) and suggests they show that NIH is worried more about scaring off the licensee than benefiting the taxpayers who funded this drug and have no assurance they won't have to pay excessively high prices for it.

-- I'm looking for an agency response to this contention.

-- My deadline is 10/28/16 at 5 PM EDT

-- My questions would basically be:
How do you respond to their complaint?
What are the institute's priorities when licensing these drugs?
How much progress has this licensee made on marketing this drug?
What were the results of the Phase I trial that NIH funded on this drug?
Some observers are asking: why grant an exclusive license to a small, unknown company with no track record of bringing drugs to market?

I'd have follow-ups depending on the answers, natch, and would want to hear any responses to smarter questions on all this that your folks might have.

Any help appreciated,

Dan Vergano

REL0000024069

b6

Dan Vergano | Science Reporter (DC) |

b6

BuzzFeed

1630 Connecticut Ave. 7th Floor,
Washington DC 20009

link: <https://s3.amazonaws.com/public-inspection.federalregister.gov/2015-06974.pdf>

Dan Vergano | Science Reporter (DC) |

b6

BuzzFeed

1630 Connecticut Ave. 7th Floor,
Washington DC 20009

On Mon, Oct 24, 2016 at 11:57 AM,
Payne, January (NIH/NIDDK) [E]
<january.payne@nih.gov> wrote:

Dear Dan,

Thanks for your message. Can you
please provide more information so I
can look into your request?

- What is the drug name, and can you please briefly describe the issue that has been raised? Also, what is the name of the public interest group?
- What is your hard deadline?
- Can you please provide a few examples of questions you'd like to ask?

Best,

January W. Payne

Office of Communications and Public
Liaison

National Institute of Diabetes
and Digestive and Kidney Diseases

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www.niddk.nih.gov

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lives and improves health*

From: Dan Vergano
[mailto:dan.vergano@buzzfeed.com]
Sent: Monday, October 24, 2016 11:25 AM
To: NIDDK NIDDKMEDIA (NIH/NIDDK)
<niddkmedia@niddk.nih.gov>
Subject: Fwd: BuzzFeed News: press
contact / licensing

Krysten's email responder suggested
I send this note to this contact. I
have also left a phone message with
the press office. I am looking for
comment this week.

Ms. Carrera,

I'm a science reporter at BuzzFeed
News. I'm looking for a press
contact at NIDDK who can address
a drug licensing issue at your
institute. A public interest group is
raising questions about one of your
licenses and I'd like to get a
response from the institute.

Thanks for any help,

Dan Vergano

BuzzFeed News

b6

Dan Vergano | Science Reporter (DC)

b6

BuzzFeed

1630 Connecticut Ave. 7th Floor,
Washington DC 20009

JANUARY PAYNE

@ National Institutes of Health

National Institutes of Health | 9000 Rockville Pike, Bethesda, MD 20892, USA | Official website (NIH). NIH is one of the world's foremost medical research centers. An agency of...



January Payne on LinkedIn



@NIH | 663K followers | 6K tweets - 3 hours ago

There's still time to submit your @NIH_LRPApplication! Get started on yours today. Deadline bit.ly/2e7QDzt#studentdebt



[Search for January Payne on Google](#)

Dan is using Senders. [View / edit your own Card](#)

<Reasonable Pricing - Virotas NIH
.pdf>

<image001.jpg>

<image001.jpg>

<image001.jpg>

<image001.jpg>

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 11/17/2017 3:19:48 PM
To: Petrik, Amy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c4ec05a179f04067b61f20605e911e7c-petrika]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: ACTION - Draft responses to FRN comments
Attachments: A-419-2017_Response to FRN inquiriesMSFandKEI MMowatt 171117.docx; A-419-2017_Response to FRN inquiries ACOG MMowatt 171117.docx

Thanks, Mark and Amy.

b5

I'll confirm when clear to send. I suggest sending pdf via email.

Mike

From: Petrik, Amy (NIH/NIAID) [E]
Sent: Friday, November 17, 2017 9:11 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: RE: ACTION - Draft responses to FRN comments

Thanks, Mark. I'll include your suggested edits to that sentence.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, November 16, 2017 5:01 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>
Subject: RE: ACTION - Draft responses to FRN comments

Good. Minor point:

b5

b5

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Thursday, November 16, 2017 4:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>
Subject: FW: ACTION - Draft responses to FRN comments

Mark,

Amy has drafted responses based on

b5

Any comments?

Thanks,

REL0000024070

Mike

From: Petrik, Amy (NIH/NIAID) [E]
Sent: Thursday, November 16, 2017 4:16 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Green, Wade (NIH/NIAID) [E] <wade.green@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: ACTION - Draft responses to FRN comments

Hi Mike,

Thanks for the update, attached are my two responses

b5

b5

I'll appreciate any suggestions and be happy to answer any questions.

Best,
Amy

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Thursday, November 16, 2017 3:52 PM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>
Cc: Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Green, Wade (NIH/NIAID) [E] <wade.green@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: ACTION - Draft responses to FRN comments

Amy,

b5

Please email me the two responses you have drafted.

I'd like you to be in a position to email out the responses to the comment providers by COB next Monday, 20 Nov.

Thanks,

Mike
Michael R. Mowatt, Ph.D.
Director, Technology Transfer and Intellectual Property Office

National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services

+1 301 496 2644



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REL0000024070

devices. National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

b5

b5

From: Francois Ravenelle [fravenelle@inversago.com]
Sent: 8/20/2018 3:26:45 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7dfe19bfd1d443ceb700b9f22d159a90-shmilovm]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: RE: KEI -T1International-NIH-InversagoPharma-20aug2018.pdf

b5

Hope this helps,

F

PS: b5

François Ravenelle, PhD
CEO & Founder
M: +1.514.922.2383
Inversago Pharma Inc

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: August 20, 2018 11:17 AM
To: Francois Ravenelle <fravenelle@inversago.com>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: KEI -T1International-NIH-InversagoPharma-20aug2018.pdf

Thank you Francois — b5

b5

Thanks!

From: Francois Ravenelle <fravenelle@inversago.com>
Sent: Monday, August 20, 2018 11:11
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: KEI -T1International-NIH-InversagoPharma-20aug2018.pdf

Duly noted,
Let me know if you feel I may be of any assistance - I am available at your convenience to discuss.
Best regards,
François

REL0000024073

François Ravenelle, PhD
CEO & Founder
M: [b6]
Inversago Pharma Inc

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: August 20, 2018 10:57 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Cc: Francois Ravenelle <fravenelle@inversago.com>
Subject: KEI -T1International-NIH-InversagoPharma-20aug2018.pdf

Dear Mark –

b5

b5

Regards,

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@nih.gov

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REL0000024073

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 1/2/2019 7:34:53 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI comment to intent to grant A-066-2019

Right, b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, January 02, 2019 2:26 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI comment to intent to grant A-066-2019

b5

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, January 02, 2019 2:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI comment to intent to grant A-066-2019

b5

Dale

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, January 02, 2019 1:50 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: Fwd: KEI comment to intent to grant A-066-2019

b5

Sent from my iPhone

Begin forwarded message:

From: "Yang, Jasmine (NIH/NCI) [E]" <jasmine.yang@nih.gov>
Date: January 2, 2019 at 1:37:45 PM EST
To: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>, "Berkley, Dale (NIH/OD) [E]" <berkleyd@od.nih.gov>
Cc: "Rodriguez, Richard (NIH/NCI) [E]" <richard.rodriguez@nih.gov>
Subject: KEI comment to intent to grant A-066-2019

Hello,

I have received the attached emails from Jaime Love of KEI in response to the following FRN <https://www.federalregister.gov/documents/2018/12/21/2018-27671/prospective-grant-of-an-exclusive-patent-license-multifunctional-rna-nanoparticles-and-methods-of>.

Attached is a draft response that I intend to respond with, pending your comments/feedback. Please let me know if anything needs to be changed to the draft and if you have any questions regarding the company, Sixfold, or the technology.

Thank you,
Jasmine

Jasmine J. Yang, Ph.D.
Sr. Technology Transfer Manager
Technology Transfer Center | National Cancer Institute | The National Institutes of Health
Riverside 5, Suite 400 | 8490 Progress Drive | Frederick, MD 21701
Email: jasmine.yang@nih.gov | (P) 301-624-8775 | (Fax) 301-631-3027
<https://techtransfer.cancer.gov/>

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<mime-attachment>

<Ltr to KEI_2019-01-02.docx>

REL0000024074

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 4/6/2018 3:29:59 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Dft Response to the University of PA
Attachments: KEI UPENN - Juxtapid Dft 04062018.docx

Mark:

I have attached a draft letter for Dr. Collin's signature in response to the University of Pennsylvania's response to the KEI request for Juxtapid.

Ann

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

b5

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 7/3/2019 5:12:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

b5

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, July 03, 2019 1:04 PM
To: Berkley, Dale (NIH/OD) [E] <berkeleyd@od.nih.gov>
Subject: RE: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

b5

From: Berkley, Dale (NIH/OD) [E] <berkeleyd@od.nih.gov>
Sent: Wednesday, July 3, 2019 12:45 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, July 03, 2019 12:27 PM
To: Berkley, Dale (NIH/OD) [E] <berkeleyd@od.nih.gov>
Subject: FW: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

b5

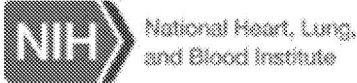
From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, July 2, 2019 9:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Pazman, Cecilia (NIH/NHLBI) [E] <pazmance@nhlbi.nih.gov>
Subject: FW: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

REL0000024077

Mark –
KEI letter with regards to my FR notice and my response.
Please comment.

Thank you,

Michael A. Shmilovich, Esq., CLP



Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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"Always be yourself....unless you can be a pyrate... then; obviously, be a pyrate"

From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Tuesday, July 2, 2019 1:31 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>
Subject: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

Dear Mr. Shmilovich:

Attached, please find Knowledge Ecology International's comments regarding the **Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063**, as well as the email correspondence referenced in the comments.

Sincerely,

Kathryn Ardizzone, Esq.
Knowledge Economy International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

REL0000024077

From: Joe Allen [jallen@allen-assoc.com]
Sent: 4/8/2019 2:21:12 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Pharma companies need to stop free riding on publicly funded research

Just came across this from The Hill (<https://thehill.com/opinion/healthcare/376574-pharmaceutical-corporations-need-to-stop-free-riding-on-publicly-funded>)

Pharmaceutical corporations need to stop free-riding on publicly-funded research

By Jason Cone, opinion contributor — 03/03/18 01:00 PM EST [42](#)



The White House Council of Economic Advisers recently announced a strategy to curb high drug prices: force “free riding” countries abroad to pay more and watch the prices go down in America.

That’s not how it works; lifesaving medicines aren’t more expensive here because they cost less elsewhere. They’re priced out of reach everywhere because pharmaceutical corporations are charging exorbitant prices simply because they can—and the U.S. government lets them.

Pharmaceutical companies have perpetuated a myth that high prices are necessary in order to compensate for the risks and investments they undertake when developing drugs. And governments like the U.S. — the biggest funder of global health research and development (R&D) — have let them.

The White House's report suggests that it costs an estimated \$2.6 billion to develop a new drug today, though they're basing this on a single, non-transparent pharmaceutical industry-supported study with problematic methodology.

In reality, companies receive substantial publicly-funded support from the government. A recent study found that all 210 drugs approved in the U.S. between 2010 and 2016 benefitted from publicly-funded research, either directly or indirectly.

Taxpayers contribute through public university research, grants, subsidies, and other incentives. This means people are often paying twice for their medicines: through their tax dollars and at the pharmacy.

At Doctors Without Borders/Médecins Sans Frontières (MSF), we see each and every day the human suffering caused in the places we work and many countries outside the U.S. by treatments being rationed or people being denied essential medical care due to high drug and vaccines prices.

We see babies in Jordan and India who have been forced to go without vaccinations against pneumonia — a disease that kills roughly one million children each year — because governments can't pay the price tags companies demand.

We hear of doctors in countries like the U.S. and Italy having to choose between patients and rationing hepatitis C medicines to only the sickest because they can't afford to treat everyone.

Making our patients pay more for their medicines, or imposing restrictions that would make them wait years for cures and innovations available to the rest of the world, won't bring down drug prices for people in the United States. Making life harder for some of the most vulnerable people in the world will not bring down drug prices in the U.S.

This administration has the power to make a difference in the lives of people struggling to pay their medical bills with meaningful reforms to the U.S. An R&D system that would benefit us all. If it is serious about bringing down drug prices, the first thing it should do is put access and affordability conditions on the public funding given to medical products in development.

If the public funds the research that led to the development of a certain medicine, there should be limits to what government will allow companies to charge consumers. It should be unacceptable for taxpayers to fund a new medicine that the public can't even afford to buy once it hits the market.

Early research on one of Swiss pharmaceutical company Novartis' best selling drugs, a cancer drug called Gleevec (imatinib) — a truly life-changing medicine for people with leukemia — was substantially funded by U.S. taxpayers through National Institutes of Health grants and support from the Leukemia Society.

This daily medication is the difference between life and death for so many people, but only if they can afford the \$97 per pill for the name-brand version or the at least \$49 for the generic option in the U.S. Additionally, the pharmaceutical industry takes all the credit for developing the breakthrough gene-altering chimeric antigen receptor T-cell (CAR T) therapy — a therapy that can cost patients \$475,000 — even though the first two CAR T treatments for multiple myeloma came out of NIH-funded research.

The U.S. government should also create better incentives to ensure the development of products that are critical for public health. For example, drug-resistant infections kill 23,000 people each year in the United States and 700,000 people globally, but it has been more than 30 years since a new class of antibiotics has been introduced.

Since antibiotics are given sparingly and for short periods of time, they attract limited interest from companies even though there is an immense need.

It's time for the U.S. to stop pitting patients against each other and get serious about promoting real innovation and lowering drug prices for everyone. This administration should start by putting an end to pharmaceutical corporations free-riding on publicly-funded research.

Jason Cone is the executive director of Doctors Without Borders, USA

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
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(c) b6
www.allen-assoc.com

From: Joe Allen [jallen@allen-assoc.com]
Sent: 6/27/2016 8:24:19 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Re: Question on the march in decision

Yikes, I was hoping that we're out of the woods. Can you say who's staffing it there? I can't imagine that they would dissent from your opinion but who knows.

On 6/27/2016 4:20 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> Nope. They have their own process.

>

> -----Original Message-----

> From: Joe Allen [mailto:jallen@allen-assoc.com]

> Sent: Monday, June 27, 2016 4:19 PM

> To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

> Subject: Question on the march in decision

>

> Just got off the AUTM public policy call and someone asked whether the NIH letter to KEI also spoke for DOD. I saw that Sec. Carter was copied on Dr Collins' letter but wasn't sure if it officially represented the views of both agencies or not. Did it?

>

> Thanks

>

>

--

Joseph P. Allen
President
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60704 Rt. 26, South
Bethesda, OH 43719
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(C) b5
www.allen-assoc.com

From: Kleinman, Joe (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A61F3DA68A824FD284D8FD06C81882B7-KLEINMANJ]
Sent: 1/8/2018 8:25:41 PM
To: Rogers, Karen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b23ef4ca2fa14a6eb174ee611953a396-rogersk]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Gottesman, Michael (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=918c2344931542a592d00dbe83d3d5a3-gottesmm]; Wyatt, Richard G (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=728cbe2fe91640be9dd1156c9c9f72f4-wyattrg]; McBurney, Margaret (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=efdfd5476a884ff7bacfb38cb2805863-mmcburney]
Subject: RE: ES - WF 369525 - FYI (CC)
Attachments: Prospective Grant of an Exclusive Patent License: The Development of an Anti-CD30 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer

FYI
Cheers,
Joe

Work Folder Information

Work Folder: WF 369525

Process: FYI

Program Analyst: Cramer, Lindsay (NIH/NCI) [E]

Due Date:

WF Subject: James Love of Knowledge Ecology International (KEI) writes Dr. Collins and Dr. David Lambertson (NCI Tech Transfer) expressing opposition to the proposed exclusive license of a portfolio of patents to Kite Pharma for chimeric antigen receptors that recognize the CLD30 protein, as posted in the Federal Register notice 82 FR 60406.

IC: od_oir

From: Love, James

To: Lambertson, DavidCollins, Francis

Remarks: FYI to: OER, CSR, OIR, OSP, OTT, and OGC. Assigned to NCI for Necessary Action (Attn: Dr. David Lambertson, NCI Tech Transfer). Please provide documentation of any action taken. Let me know if you have any questions. Thank you! - Lindsay

Additional instructions are included on the task form, click the link to open the [Task](#)

From: James Love [james.love@keionline.org]
Sent: 1/4/2018 10:04:08 PM
To: NIH Executive Secretariat [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7af5a3e94af34fd592e0fe4ab24c4bad-odexecsec1]; Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]; Kochenderfer, James (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ba7cd3e23bef4385a97dd7f4d644072c-kochendj]
CC: Andrew S. Goldman [andrew.goldman@keionline.org]; Manon Ress [manon.ress@keionline.org]; Diane Singhroy [diane.singhroy@keionline.org]; Kim Treanor [kim.treanor@keionline.org]; Claire Cassedy [claire.cassedy@keionline.org]; Thiru Balasubramaniam [thiru@keionline.org]
Subject: Prospective Grant of an Exclusive Patent License: The Development of an Anti-CD30 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer
Attachments: KEI-KITE-CAR-T-NIH-4Jan2018.pdf
Flag: Follow up

Dr. Francis Collins, M.D., Ph.D., Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892
Email: execsec1@od.nih.gov

David A. Lambertson, Ph.D., Senior Technology
Transfer Manager, NCI Technology Transfer Center,
Rockville, MD 20850-9702
Email: david.lambertson@nih.gov.

Dear Director Collins and Dr. Lambertson:

Knowledge Ecology International (KEI) is writing to express our opposition to the proposed exclusive license of a portfolio of patents to Kite Pharma, since October a wholly-owned subsidiary of Gilead, for chimeric antigen receptors that recognize the CLD30 protein, as posted in the Federal Register notice [82 FR 60406](#).

We object to the granting of the exclusive license, and request that if the NIH proceeds with the license, public interest safeguards are included.

Our comments are included in the attached PDF file.

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,

twitter.com/jamie_love



January 4, 2017

Dr. Francis Collins, M.D., Ph.D., Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892
Email: execsec1@od.nih.gov

David A. Lambertson, Ph.D., Senior Technology
Transfer Manager, NCI Technology Transfer Center,
Rockville, MD 20850-9702
Email: david.lambertson@nih.gov

Dear Director Collins and Dr. Lambertson:

Knowledge Ecology International (KEI) is writing to express our opposition to the proposed exclusive license of a portfolio of patents to Kite Pharma, since October a wholly-owned subsidiary of Gilead, for chimeric antigen receptors that recognize the CLD30 protein, as posted in the Federal Register notice [82 FR 60406](#).

We object to the granting of the exclusive license, and request that if the NIH proceeds with the license, public interest safeguards are included.

1. Background

The Federal Register notice identified several forms of cancer that may be treated with the technology, including Hodgkin's Lymphoma (HL), Non-Hodgkin's Lymphoma (NHL), diffuse large B cell lymphoma (DLBCL), peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), anaplastic large cell lymphoma (ALCL), and angioimmunoblastic T-cell lymphoma (AITL).

The inventor listed in the patent applications referred to in the Federal Register notice is James N. Kochenderfer, M.D.

The technology to be licensed appears to be undergoing an NIH funded Phase 1 trial with the ClinicalTrials.gov identifier: [NCT03049449](#).

The NIH proposed worldwide rights, and has filed a patent application with the WIPO PCT seeking protection in the following countries:

Pub. No.: WO/2017/066122
International Application No.: PCT/US2016/056262
Publication Date: 20.04.2017
International Filing Date: 10.10.2016
Applicants: THE UNITED STATES OF AMERICA, AS REPRESENTED
BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN
SERVICES [US/US]; Office of Technology Transfer National Institutes
of Health
Inventors: KOCHENDERFER, James N.

Designated States:

AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC,
EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,
IS, JP, KE, KG, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA,
MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG,
SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, ZA, ZM, ZW.

African Regional Intellectual Property Organization (BW, GH, GM, KE,
LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW)

Eurasian Patent Organization (AM, AZ, BY, KG, KZ, RU, TJ, TM)

European Patent Office (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO,
PL, PT, RO, RS, SE, SI, SK, SM, TR)

African Intellectual Property Organization (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

2. It is premature to grant an exclusive license, given the fact that the NIH is funding a Phase 1 trial.

We object to the NIH licensing this promising technology before the patent has been granted, and before the NIH concludes and evaluates the results from the ongoing Phase 1 trial, which

began on March 17, 2017 and currently has an estimated primary completion date of June 30, 2021, according to the NIH database ClinicalTrials.Gov.

In an environment where there is widespread alarm over the escalating costs of treatments for cancer and Congressional concerns over the pricing of NIH-funded biomedical inventions, it is unwise for the NIH to create a monopoly on this NIH-funded invention, before the NIH can evaluate both the evidence from the ongoing Phase 1 trial and the costs of moving the technology forward to FDA approval, if the Phase 1 results are encouraging.

Evaluating the costs of obtaining FDA approval would entail a comparison of the costs that the NIH would incur directly if it were to conduct the result itself, versus the costs imposed on U.S. patients, employers and taxpayers if the NIH grants a legal monopoly to Gilead.

If the costs of the NIH funding the R&D itself directly leads to significant savings over the costs to U.S. residents of granting a legal monopoly, the NIH should not grant the monopoly.

3. If the NIH grants an exclusive license, it should include clear safeguards in the license to protect U.S. residents from excessive prices and access barriers.

- a. The price should not discriminate against U.S. residents.

At a very minimum, the NIH should include a provision in the licenses that would ensure that the price for a product or service that relied upon the invention would not be more expensive in the United States than the median price charged for a group of countries that include Canada plus the eight largest economies in the world that also have a nominal per capita income at least 50 percent of that of the United States (as measured by GNI, World Bank Atlas method).

- b. The price should not constitute an unreasonable barrier to access in the United States.

If there is a significant gap between the number of patients who would benefit from the treatment and the number of patients who receive the treatment, the monopoly should be terminated.

- c. The price should not be higher than CAR T treatments of similar efficacy, taking into account differences in patient populations, if the cumulative revenue per indication is less than \$300 million.

We note that the two previous CAR T procedures approved by the FDA involved a small number of patients in trials, including, for example, Yescarta, also licensed by the NIH to Gilead/Kite, whose FDA press release stated “The safety and efficacy of Yescarta were established in a multicenter clinical trial of more than 100 adults . . .”

- d. The price should not increase faster than the rate of inflation as measured by the consumer price index, unless the increase can be justified by a need to earn a reasonable profit on the risk adjusted investments in research and development.

Alternatively, if revenues are robust, there could be a requirement that prices decline as companies reach certain benchmarks.

- e. The revenues earned under exclusive rights should not be excessive.

When the cumulative global revenue for the product exceeds a particular benchmark, the monopoly should end. We recommend the benchmark for this product be \$300 million, for each approved FDA indication, or \$1 billion for all indications.

4. The NIH should protect patients in countries with per capita incomes that are less than one third of U.S. per capita income.

The NIH should either limit the exclusive rights to countries that have at least one third U.S. per capita income, as measured by the World Bank Atlas method GNI per capita, or place requirements that products in such countries be affordable.

5. The NIH should require transparency with regards to R&D outlays.

It is an unnecessary and reason-inhibiting fact that actual R&D outlays are often hidden from the public, although speculation about R&D costs is used to justify high prices. The NIH can remedy this by requiring that companies that license NIH-owned technologies disclose to the public the actual R&D costs for commercializing inventions, along with all public sector R&D subsidies, such as the Federal R&D and Orphan Drug tax credits.

Sincerely,



James Love
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009
<http://keionline.org>
james.love@keionline.org

Cc:

James N. Kochenderfer, M.D.

Center for Cancer Research

National Cancer Institute

Bethesda, MD 20892

kochendj@mail.nih.gov

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 6/27/2018 6:12:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Kirby, Tara (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2368a591fa4c4932a802e5d467fb49ed-tarak]; Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]; Sayyid, Fatima (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b9e45041bdb43719f7113a5aae27057-sayyidf]; Soukas, Peter (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b1f6020157ac47948c6e34166b78e433-soukasp]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]
Subject: RE: Example response to FRN query
Attachments: a-257-2018_Response to KEI MLR final.docx

SENSITIVE AND PRIVILEGED – NOT FOR DISTRIBUTION

Mark,

b5

Sharing this with my team for their awareness.

Mike

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, June 27, 2018 1:47 PM
To: Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Subject: RE: Example response to FRN query

b5

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Wednesday, June 27, 2018 1:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Example response to FRN query

FYI, Peter's response to the RSV license a few years back.

From: Soukas, Peter (NIH/NIAID) [E]
Sent: Tuesday, March 22, 2016 4:33 PM
To: 'Jamie Love' <james.love@keionline.org>
Subject:

REL0000024084

Dear Mr. Love,

We write to confirm receipt of your comments (dated March 8, March 4, and February 22, 2016) regarding the Federal Register Notice at F.R. Vol. 82, No. 34 (page 8728), published on Monday, February 22, 2016. NIH considers all written comments received in response to notices. When making a final determination to grant an exclusive patent license, NIH complies with the statutes and regulations for licensing inventions, including 37 C.F.R. section 404.7, and determines that the public will be served by the granting of the license, that an exclusive or partially exclusive license is reasonable and necessary, and that the proposed scope of exclusivity is not greater than reasonably necessary.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Technology Transfer and Intellectual Property Office
Suite 6D
5601 Fishers Lane, MSC9804
Rockville, MD 20852-9804
Phone: 301-594-8730
Fax: 240-627-3117
Email: ps193c@nih.gov
<http://www.niaid.nih.gov/LabsAndResources/techDev/Pages/default.aspx>



22 June 2018

VIA E-MAIL ONLY

James Love
Knowledge Ecology International
1621 Connecticut Ave. NW, Suite 500
Washington, DC 20009

IN RE: Prospective Grant of an Exclusive License (NIH License Application A-257-2018) to Morphiex Biotherapeutics, published on 15 May 2018 in *Federal Register* Vol. 83, No. 94, page 22501.

Dear Mr. Love:

Thank you for providing us with your comments regarding the notice of the proposed license to Morphiex Biotherapeutics (Morphiex) by the National Cancer Institute (NCI).

Prior to posting a notice for a proposed grant of an exclusive license, the NCI has reviewed the company's business development plan and other available information and determined that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) have been satisfied and that the company is qualified both technically and financially to be granted an exclusive license to the Government's intellectual property in the fields of use as specified. The notice period provides an opportunity for public comment and possible objection to the proposed license. We consider all comments prior to negotiating the proposed license.

Your comments have been given full consideration, but your opposition to the grant of an exclusive license to Morphiex for NCI technology E-227-2006 in the limited field of use that has been advertised is not found persuasive to deter the NCI from entering into negotiations with the company. NCI grants licenses pursuant to the requirements of 37 CFR 404.7. . You state that the company does not have a website. We would refer you to an internet search from which one can find their facebook page <https://www.facebook.com/morphiex/> and their linkedin page <https://www.linkedin.com/company/morphiex/>, which refers to their website www.morphiex.com, and well as that website appearing in the internet search. We are not able to provide business confidential information from their business plan. Further, with regard to your comments about transparency, your organization is welcome to submit requests for documents; such requests should be filed under the Freedom of Information Act. The webpage for the NIH FOIA Office provides more information on filing requests: www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedom-information-act-office/submitting-foia-requests. Note that under 35 USC sec 209, the business development plan submitted by a prospective licensee "shall be treated by the Federal agency as commercial and financial information obtained from a person and privileged and confidential and not subject to disclosure under section 552 of title 5."

In conclusion, NCI has determined that your objection did not raise an issue that would preclude the grant of the proposed exclusive license, and the NCI intends to proceed with the negotiation of the proposed exclusive license, the terms of which have not yet been negotiated. All of the regulations and statutes governing the grant of an exclusive license have been adhered to during the evaluation of the Morphiex license application.

Sincerely,
Jaime M. Greene, M.S.
Senior Technology Transfer Manager
National Cancer Institute, TTC



greenajaime@mail.nih.gov

From: Berkley, Dale (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=BERKLEYD]
Sent: 6/16/2017 7:48:00 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Dodson, Sara (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Dodsonse]
Subject: RE: Your CRISPR comments
Attachments: WF365656 KEI Response OEROSP (002)--OGCBerkleyComments.docx

Here it is. Let me know if you want me to send a clean copy, etc., or drop it into the body of the email.

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, June 16, 2017 3:46 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Dodson, Sara (NIH/OD) [E] <sara.dodson@nih.gov>
Subject: Your CRISPR comments

Dale:

I cannot pull up your edited doc on my phone now. Could you please resend your edits to me and Sara.

Thanks
Mark

Sent from my iPhone

b5

b5

Lili M. Portilla, MPA
Director, Strategic Alliances
National Center for Advancing Translational Sciences (NCATS), NIH
P: 301-217-2589
E: Lilip@nih.gov

FYI

Thank you for your response. I have already contact Kevin Chang but he suggested I write to the inventors. Are you unable to discuss the paper?

Elizabeth

On Fri, Apr 17, 2015 at 1:40 PM, Marugan, Juan (NIH/NCATS) [E] <maruganj@mail.nih.gov> wrote:

Thank you for your email. All inquiries regarding this technology should be referred to Dr. Kevin Chang at the NIH OTT. His contact info is listed below.

REL0000024087

Kevin W. Chang, Ph.D.

Senior Licensing and Patenting Manager

NIH Office of Technology Transfer

6011 Executive Blvd, Suite 325

Rockville, MD 20852

Phone: (301) 435-5018

Fax: (301) 402-0220

Regards,

Juan Marugan

From: elizabeth.rajasingh@gmail.com [mailto:elizabeth.rajasingh@gmail.com] **On Behalf Of** Elizabeth Rajasingh

Sent: Friday, April 17, 2015 10:49 AM

To: Marugan, Juan (NIH/NCATS) [E]

Subject: Questions Re: Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection

Hi Dr. Marugan,

I work for Knowledge Ecology International, an NGO which advocates for, among other things, greater access to affordable medicines worldwide.

I read your article titled, "Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection." I have worked on the issue of access to medicines for Hepatitis C patients for many months now and am interested in your research, especially as a potential new low-cost treatment for HCV.

REL0000024087

Can I give a call to learn more about your research, its potential, and the licensing of the patents involved in it?

Thank you very much,

Elizabeth Rajasingh

Elizabeth Rajasingh

Perls Research and Policy Fellow, Knowledge Ecology International

1621 Connecticut Ave. NW, Suite 500

Washington, DC 20009

elizabeth.rajasingh@keionline.org | 1-202-332-2670

From: Lambertson, David (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=3C95B34F709746A8A2553CE54E74ACE2-LAMBERTSOND]
Sent: 7/15/2019 5:09:39 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

b5

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702
Bethesda, MD 20892-9702 (USPS)
Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 15, 2019 12:59 PM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: Re: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

b5

Sent from my iPhone

On Jul 15, 2019, at 12:05 PM, Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov> wrote:

Sure I can do that. I have attached a draft response for your consideration. Let me know if you or Dale have any changes you would like to see before I send the response.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager

REL0000024088

Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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Bethesda, MD 20892-9702 (USPS)
Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 15, 2019 11:38 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

b5

From: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Sent: Monday, July 15, 2019 11:25 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Hi Mark,

b5

Once I hear back from you I can draft a response for review by you and Dale before I send it.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

REL0000024088

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Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 15, 2019 11:07 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Thanks, [REDACTED] b5

[REDACTED] b5

Does that work?

From: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Sent: Monday, July 15, 2019 10:13 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Good morning Mark,

[REDACTED] b5

b5 Please let me know if there is a general response we should provide to them or if there is some alternative approach you would like to take.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702
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Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
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Fax: 240-276-5504

REL0000024088

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From: Claire Cassedy <claire.cassedy@keionline.org>
Sent: Friday, July 12, 2019 2:04 PM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Dear Dr. Lambertson,

I am writing in reference to the Federal Register notices 84 FR 33272 and 84 FR 33270 regarding, "Prospective Grant of an Exclusive Patent License: Autologous Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20" and "Prospective Grant of an Exclusive Patent License: Allogeneic Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20," for which you are listed as the contact for inquiries. I was hoping you could provide me with some further information regarding the status of the technologies.

1. At what stage of development are the inventions listed?
2. Has the government funded any clinical trials relevant to these technologies?
3. If the government has provided funding, how much has been spent by the government on these trials? Can you provide NCT numbers?
4. Is the term in the proposed licenses to be life of patent or less than life of patent?
5. In working towards executing this license, has the NIH sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the "disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law"?
6. Considering the NIH has previously licensed CAR T technologies to Kite Pharma/Gilead, are the technologies identified in the current Federal Register notice related in any way to the previously executed licenses? (*List of previously noticed exclusive licenses on CAR T technologies to Kite Pharma follows below this email*)
7. Is there a Cooperative Research and Development Agreement associated with this technology?
8. Did the NIH previously post this technology in the Federal Register under "Government Inventions available for licensing"? And/or was it announced on any other platform that these technologies were available for licensing?
9. If not, how was it determined that Kite would enter into this proposed exclusive license, particularly considering the technology is currently under a provisional patent application?
10. Considering Kite/Gilead currently has CAR T therapy Yescarta (axicabtagene ciloleucel) on the market at a price of \$373,000, has/will the NIH seek license terms that will ensure the resultant therapy is available to patients on reasonable terms?

Thank you in advance for your assistance in this matter.

Sincerely,

Claire Cassedy

Previously noticed exclusive licenses on CAR T technologies to Kite Pharma:

Prospective Grant of Exclusive License: Development of T Cell Receptors and Chimeric Antigen Receptors Into Therapeutics for Adoptive Transfer in Humans To Treat Cancer
<https://www.federalregister.gov/documents/2012/01/24/2012-1383/prospective-grant-of-exclusive-license-development-of-t-cell-receptors-and-chimeric-antigen>

Prospective Grant of Exclusive License: Development of T Cell Receptors for Adoptive Transfer in Humans to Treat Cancer
<https://www.federalregister.gov/documents/2014/03/25/2014-06412/prospective-grant-of-exclusive-license-development-of-t-cell-receptors-for-adoptive-transfer-in>

Prospective Grant of Exclusive License: Development of T Cell Receptors for Adoptive Transfer in Humans To Treat Cancer

<https://www.federalregister.gov/documents/2014/10/16/2014-24502/prospective-grant-of-exclusive-license-development-of-t-cell-receptors-for-adoptive-transfer-in>

Prospective Grant of Exclusive License: The Development of an Anti-CD19 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancers

<https://www.federalregister.gov/documents/2015/06/26/2015-15657/prospective-grant-of-exclusive-license-the-development-of-an-anti-cd19-chimeric-antigen-receptor-car>

Prospective Grant of Exclusive Patent License: Development of T Cell Receptors (TCRs) Targeting the KRAS G12D Mutation for the Treatment of Cancer

<https://www.federalregister.gov/documents/2016/08/17/2016-19549/prospective-grant-of-exclusive-patent-license-development-of-t-cell-receptors-tcrs-targeting-the>

Prospective Grant of Exclusive Patent License: Development of Anti-CD70 Chimeric Antigen Receptors for the Treatment of CD70 Expressing Cancers

<https://www.federalregister.gov/documents/2016/10/05/2016-24030/prospective-grant-of-exclusive-patent-license-development-of-anti-cd70-chimeric-antigen-receptors>

Prospective Grant of an Exclusive Patent License: The Development of an Anti-CD30 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer

<https://www.federalregister.gov/documents/2017/12/20/2017-27416/prospective-grant-of-an-exclusive-patent-license-the-development-of-an-anti-cd30-chimeric-antigen>

--

Claire Cassidy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

<Proposed KEI Response.docx>

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 1/2/2019 4:10:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Ferguson, Steve (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=aec79b088ce947819eadd4bf420aa54b-fergusos]; Rogers, Karen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b23ef4ca2fa14a6eb174ee611953a396-rogersk]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]; Harbinger, Bonny (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f5f21b431a114600bca14696e985e801-harbingb]
Subject: RE: Question from DOJ

b5

Richard

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 2, 2019 10:57 AM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Ferguson, Steve (NIH/OD) [E] <FERGUSOS@od6100m1.od.nih.gov>; Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Harbinger, Bonny (NIH/OD) [E] <harbingb@od.nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: Question from DOJ

b5

Thanks

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

REL0000024089

From: Joe Allen [jallen@allen-assoc.com]
Sent: 4/6/2018 3:20:11 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Advocacy groups urge HHS to seize Sarepta patent under Bayh-Dole

Here's the latest attack from today's Endpoint News:

Should Sarepta's patents be seized by the government? Patient advocates pitch controversial drug pricing proposal

Six advocacy groups are sending a big ask to the federal government to lower the price of one rather expensive drug for Duchenne muscular dystrophy, petitioning health regulators to flex power it's never exercised before.

Amidst a years-long debate over drug pricing, Sarepta has hit a sensitive chord with the high price tag of its DMD drug Exondys 51 (eteplirsen), which goes for a around \$300,000 per year.

The organizations drafted a letter to the Department of Health and Human Services (HHS), pleading that Secretary Alex Azar act to lower the price of the drug. Specifically, the group wants HHS to leverage a piece of legislation called the Bayh-Dole Act — along with contractual agreements with funding agencies — to take over ownership of five patents on Exondys 51. They can do that, the group insists, because the intellectual property was backed by federal research dollars. Grant recipients are required to disclose federal funding that contributes to a patented invention on their patent application — a step that both Sarepta and the University of Western Australia failed to do.

By taking title to the patents, the HHS could leverage their position to lower the price of Exondys, the organizations said.

Analysts at Leerink, who cover Sarepta's stock \$SRPT, sent a note to investors this morning noting the unlikelihood that such action would be taken by the government.

“Bottom Line: Today's letter from several groups delivered to HHS Secretary (Alex) Azar highlights the lengths that some are willing to go in order to force drug prices lower; however we believe these groups have an uphill battle, and even if they were to prevail there would be limited read through to other rare disease companies whose business models rely on premium pricing.”

Leerink reminds investors that a similar strategy was used against Gilead, Vertex, and Novartis, among others. Those efforts failed.

The letter writers acknowledge the action they're requesting is unprecedented:

In the past, the federal government has, on several occasions, asked recipients of federal grants and contracts to correct failures to disclose federal funding of the inventions, but has not exercised its rights to take the title of such patents for purposes of influencing drug prices. In this respect, we recognize that we are asking HHS to do something new.

And later, the letters sound rather hopeless:

We respectfully ask for a meeting with your staff to further discuss this issue, noting that as a practical matter, if the decisions are delegated solely to the NIH (Office of Technology Transfer) staff it is highly unlikely any action will be taken to moderate the price of this drug.

Read the full letter here, written and submitted by KEI, Health GAP, Patients for Affordable Drugs, People of Faith for Access to Medicines, Social Security Works and Universities Allied for Essential Medicines.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Joe Allen [jallen@allen-assoc.com]
Sent: 4/7/2019 3:35:04 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Jamie Love's letter to Congress opposing NIST Bayh-Dole proposals

Here we go:

Open letter on NIST Draft Green Paper on Bayh-Dole Act Policies and Regulations

Posted on [April 5, 2019](#) by [Claire Cassedy](#)

Open letter on NIST Draft Green Paper on Bayh-Dole Act Policies and Regulations

5 April 2019

FMI: Claire Cassedy, claire.cassedy@keionlineorg +1.202.332.2670

Washington, 5 April 2019 – Eleven non-governmental organizations have sent a letter to members of the US Congress, highlighting an emerging threat to the public safeguards in the Bayh-Dole Act.

A copy of the letter is attached below, and available via PDF [here](#).

[Letter-NIST-Bayh-Dole-GreenPaper-5April2019](#)

Signatories to the letter include:

Health GAP
Housing Works
Knowledge Ecology International (KEI)
Médecins Sans Frontières(MSF)/Doctors Without Borders USA
Public Citizen
Social Security Works (SSW)
The Institute for Agriculture and Trade Policy (IATP)
Union for Affordable Cancer Treatment (UACT)
UNITE HERE
Universities Allied for Essential Medicines (UAEM)
Yale Global Health Justice Partnership

Background

The National Institute of Standards and Technology (NIST), which falls under the Department of Congress, has advanced a draft Green Paper (NIST Special Publication 1234) that would significantly narrow the definitions of the terms laid out in the Bayh-Dole Act that give the government the ability to ensure that the public has affordable access to effective medicines or otherwise promote competition or expand use for any government funded invention.

At a time when drug prices have become increasingly unaffordable for American patients, the administration's proposals in the NIST paper outline provisions designed to protect pharmaceutical companies that sell expensive treatments, and exempt them from obligations to ensure that treatments are affordable and accessible.

The open letter describes the proposals in the draft Green Paper that, if allowed to move forward, will risk three major public safeguards against high drug prices: the federal government's royalty-free and march-in rights to inventions whose development it funded, as well as the obligation that federally-funded inventions be made "available to the public on reasonable terms."

The final version of the Green Paper is set to be released this month, and following its release, NIST will seek to initiate implementation actions, including proposed legislation and regulation processes as laid out in the Green Paper.

The letter signed by eleven NGOs seeks to call Congress' attention to this underhanded gutting of public safeguards on drug prices.

The text of the NGO letter is as follows:

April 5, 2019

Dear Members of Congress,

We are writing to draw your attention to proposals recently published by the National Institutes of Standards and Technology (NIST) that are designed to limit the government's rights in patented inventions. In particular, NIST is proposing regulations that would greatly narrow the government's ability to curb excessive prices on drugs and other technologies that were invented on federal grants and research contracts.

The proposals have emerged from a little publicized review of relatively uncontroversial aspects of licensing practices by federal labs. During workshops, licensing offices for universities and other research institutions made proposals to gut the public interest safeguards in the federal Bayh-Dole Act for patented inventions.

In December 2018, NIST published a draft Green Paper on its webpage, (NIST Special Publication 1234, <https://doi.org/10.6028/NIST.SP.1234>) with the misleading title: "Return on Investment Initiative for Unleashing American Innovation." A public comment period was only noticed on a NIST webpage that was unavailable during the government shut down.

At a time when drug prices have become increasingly unaffordable for American patients, the administration's proposals in the NIST paper outline provisions designed to protect pharmaceutical companies that sell expensive treatments, and exempt them from obligations to ensure that treatments are affordable and accessible.

If the proposals in the draft Green Paper are allowed to move forward, three major safeguards written into the Bayh-Dole Act are at risk.

- The federal government's royalty-free right to inventions whose development it funded (as mandated under 35 USC § 202 and 35 USC § 209), would be narrowed to exclude the ability to use the royalty-free right when the government does "does not directly use or consume" the patented goods and services. This change would prevent the government from using the royalty-free right to provide affordable drugs to Medicare, the Ryan White program or other government programs.

- March-in rights on federally-funded inventions (under 35 USC § 203) would be limited to cases where there is a “compelling national issue or declared national emergency” and would never be available in cases to curb excessive prices on government funded inventions.
- The obligation to bring federally-funded inventions to practical application, including in particular the requirement that the benefits of the inventions be made “available to the public on reasonable terms,” would be defined so that “reasonable terms” would never include the price that the public pays.

These proposed changes are motivated by efforts to protect drug companies from increasing demands from members of Congress and the public to use the Bayh-Dole rights to curb excessive prices for treatments for cancer, HIV and other diseases. They will also apply to other areas where the federal government research funding is significant, including for example, for new energy and information technologies.

We believe that when public resources contribute to a collective effort to develop a technology, the government has an additional responsibility to ensure that the public can benefit from those efforts.

The final version of the Green Paper is expected to be released soon. Following its release, NIST will seek to initiate implementation actions, including proposed legislation and regulation processes as laid out in the Green Paper.

We are opposed to any effort to undermine the public interest safeguards in the Bayh-Dole Act.

Sincerely,

Organizations (in alphabetical order)

Health GAP
Housing Works
Knowledge Ecology International (KEI)
Médecins Sans Frontières(MSF)/Doctors Without Borders USA
Public Citizen
Social Security Works (SSW)
The Institute for Agriculture and Trade Policy (IATP)
Union for Affordable Cancer Treatment (UACT)
UNITE HERE
Universities Allied for Essential Medicines (UAEM)
Yale Global Health Justice Partnership

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[Access to Medicine](#), [Government Funded research](#) [Bayh-Dole Act](#), [NIST](#)

Post navigation

[Structure of an Access to Knowledge Treaty. The KEI intervention at SCCR 38, on copyright limitations and exceptions](#)

[Comment on Damages provisions in USMCA IP Chapter, as regards biologic drugs, and patents on surgery and medical procedures](#)

--

Joseph P. Allen
President

Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Lambertson, David (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=3C95B34F709746A8A2553CE54E74ACE2-LAMBERTSOND]
Sent: 6/11/2018 2:52:50 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: RE: BEORO Therapeutics license

I'm fine with that, as well. I will send a response on to Dale in the next few minutes, with a copy to you both.

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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Fax: 240-276-5504

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, June 11, 2018 10:49 AM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: RE: BEORO Therapeutics license

b5

From: Rodriguez, Richard (NIH/NCI) [E]
Sent: Monday, June 11, 2018 10:45 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: BEORO Therapeutics license

Fine by me.

From: Lambertson, David (NIH/NCI) [E]
Sent: Monday, June 11, 2018 10:43 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Rodriguez, Richard (NIH/NCI) [E]

<richard.rodriguez@nih.gov>

Subject: FW: BEORO Therapeutics license

Please see my proposed responses below in red. I will forward to Dale once we are all on board with the response.

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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From: James Love [mailto:james.love@keionline.org]
Sent: Thursday, June 07, 2018 5:00 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: BEORO Therapeutics license

David A. Lambertson, Ph.D.,
Senior Technology Transfer Manager,
NCI Technology Transfer Center
Email:

david.lambertson@nih.gov.

David, we intend to file comments on this license. Below is a draft of what we will file, probably with other groups. We would like to call to explain the motivation for these various requests, including the transparency proposals.

Also, can you answer a few questions about the license.

1. What is the proposed consideration for the exclusive license? b5
2. Are there any former NIH employees involved with the company? b5
3. Does this company have a track record of developing new drugs or treatments? b5
b5
4. Will the company manufacture or conduct research in the United States. b5
b5
5. Did the NIH do any analysis to see if a term that is less than the life of a patent would be appropriate and sufficient? b5
6. Did the NIH ask DOJ for a review, under 40 USC 559? b5
b5

Jamie

Knowledge Ecology International (KEI), , and _____ are organizations concerned about drug pricing and access to patented medicines, offering comments on the grant of an exclusive license, between the National Institutes of Health (NIH) and

BEORO Therapeutics, GmbH. ("Beoro") located in Seefeld, Germany, for patents noticed in the Federal Register (83 FR 26487) the Development of an Anti-BCMA Immunotoxin for the Treatment of Human Cancer.

(See: <https://www.gpo.gov/fdsys/pkg/FR-2018-06-07/pdf/2018-12179.pdf>)

The above entities oppose the issuing of the license unless:

A. The NIH has determined that an exclusive license is "a reasonable and necessary incentive" to induce investments for the development and practical application of the invention, as is required by 35 USC § 209, and shares its analysis with the public; and

B. The NIH limits the scope of rights for the exclusivity to only those rights reasonably necessary to induce investments for the development and practical application of the invention, and in particular, that the field of use is sufficiently narrow, that the term of the exclusivity is sufficiently limited, and that the license contains sufficient safeguards to ensure that the invention is "available to the public on reasonable terms," as is required by 35 USC § 209 and 35 USC § 201(f).

Our comments address three areas of concern, (1) the pricing, affordability and access issues, (2) freedom for researchers to use the inventions, and (3) requirements for transparency of the development and commercialization of the medicine.

We propose the following safeguards regarding the pricing of and access to products that use the inventions:

1.

Products are priced no higher in the United States than the median price charged in the seven largest economies as measured by nominal GNI that have a nominal GNI per capita of at least 50 percent of the United States. To fully appreciate our concerns about the discriminatory pricing that makes US residents pay more than everyone else, please review the cross country price comparisons here: <http://drugdatabase.info/drug-prices/>

2.

Prices for products in the United States do not exceed the estimated value of the treatment, as determined by independent health technology assessments selected by Department of Health and Human Services (HHS).

3.

Patient co-payments under third party Medicare and private reimbursement programs are affordable.

4.

The geographic area for the exclusivity should exclude countries with a per capita income less than 30 percent that of the United States. If there is no such exclusion, the company be required to report annually on the reasonable and feasible measures that will be taken to ensure access to patients living in such countries. Here, please note the data from <http://drugdatabase.info/drug-prices/>, which shows that in many developing countries, prices are frequently higher than the prices for high income countries in Europe, despite the much lower per capita income in developing countries (including for taxpayer funded cancer drugs), illustrating the need for a policy to be included in NIH licenses. We also note the Medicines Patent Pool (MPP) has recently announced it will expand the scope of diseases for

its licenses. The NIH should retain the flexibility to provide licenses to the MPP in the future, perhaps as an option clause in the license.

5.

The initial period of exclusivity is set at seven years, subject to extensions if the company can demonstrate it has not recovered sufficient profits given the risk-adjusted value of the clinical trials used to register similar drugs for the lead indication.

6.

Absent satisfaction of the requirements of proposed safeguard number 5, the exclusivity of the product be reduced when cumulative global revenues for the product exceed \$1 billion, by one year for every \$0.5 billion in cumulative sales that exceed \$1 billion in cumulative sales.

The NIH might consider a different set of benchmarks than \$1 billion and \$.5 billion. In considering any benchmarks for global sales benchmarks, note that the licensing of inventions to the company significantly reduces the company's costs of preclinical research, which various studies have estimated to be 40 to 55 percent of drug development costs on a risk- and capital cost-adjusted basis.

To address research by third parties on the patented invention, we propose the NIH explicitly permit researchers worldwide to use the inventions for research purposes, regardless of whether or not research has a grant or contract from a U.S. government agency, and for both profit or non-profit organizations.

To address transparency, we proposes the company be required to provide an annual report for the public providing disclosures of the following items:

1.

The amount of money R&D to obtain FDA and foreign government approvals of the inventions, including in particular, the amount of money spent each year on each trial, and the relevant tax credits, grants and other subsidies received from any government or charity relating to those R&D outlays,

2.

The prices and revenue for the products, by country,

3.

The number of units sold, in each country,

4.

The product-relevant patents obtained in each country, and

5.

The regulatory approval obtained in each country.

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: Ekweani, Elonna (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E57D5FB210184B3C905698FE63EE1F1D-EKWEANIEJ]
Sent: 6/27/2018 8:50:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion

Interesting read. Thank you for sharing.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 26, 2018 12:30 PM
To: Ekweani, Elonna (NIH/OD) [E] <elonna.ekweani@nih.gov>
Subject: FW: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion

FYI

b5

From: Berkley, Dale (NIH/OD) [E]
Sent: Tuesday, June 26, 2018 11:58 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion

Attached is KEI's response to our motion to dismiss, just for your information. ~~no action necessary~~. Please distribute to any others in management who have an interest or need to know.

b5

b5

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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REL0000024097

From: Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=JORGENSONLA]
Sent: 6/16/2017 7:40:06 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: final memo to FC on royalties

I was just on the phone with her. b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, June 16, 2017 3:30 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: final memo to FC on royalties

b5

Sent from my iPhone

On Jun 16, 2017, at 3:09 PM, Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV> wrote:

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
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Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, June 16, 2017 3:07 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: final memo to FC on royalties

b5

Sent from my iPhone

On Jun 16, 2017, at 11:26 AM, Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV> wrote:

Attached are a few edits and comments for your consideration.

REL0000024099

Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Friday, June 16, 2017 10:07 AM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: final memo to FC on royalties

Hi Dale,

Let me apologize in advance for being needy— I believe Mark Rohrbaugh sent you a copy of this draft response to KEI regarding CRISPR royalties. We are trying to get it under Francis' review today before Carrie leaves town. Did you have a chance to review?

Again – I apologize for the turn around.

Best,

Lyric

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, May 15, 2017 3:19 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Subject: final memo to FC on royalties

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

<WF365656 KEI Response OEROSP (002)--OGCBerkleyComments.docx>

REL0000024099

From: Lambertson, David (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=3C95B34F709746A8A2553CE54E74ACE2-LAMBERTSOND]
Sent: 7/15/2019 4:05:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite
Attachments: Proposed KEI Response.docx

Sure I can do that. I have attached a draft response for your consideration. Let me know if you or Dale have any changes you would like to see before I send the response.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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Fax: 240-276-5504

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 15, 2019 11:38 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

b5

From: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Sent: Monday, July 15, 2019 11:25 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Hi Mark,

b5

b5

Once I hear back from you I can draft a response for review by you and Dale before I send it.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 15, 2019 11:07 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: RE: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Thanks,

b5

b5

Does that work?

From: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Sent: Monday, July 15, 2019 10:13 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Good morning Mark,

b5

Please let me know if there is a general response we should provide to them or if there is some alternative approach you would like to take.

Thanks,
Dave

David A. Lambertson, Ph.D.

REL0000024100

Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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From: Claire Cassedy <claire.cassedy@keionline.org>
Sent: Friday, July 12, 2019 2:04 PM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: Inquiry re: Proposed Exclusive Licenses on CD19 and CD20-related therapies to Kite

Dear Dr. Lambertson,

I am writing in reference to the Federal Register notices 84 FR 33272 and 84 FR 33270 regarding, "Prospective Grant of an Exclusive Patent License: Autologous Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20" and "Prospective Grant of an Exclusive Patent License: Allogeneic Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20," for which you are listed as the contact for inquiries. I was hoping you could provide me with some further information regarding the status of the technologies.

1. At what stage of development are the inventions listed?
2. Has the government funded any clinical trials relevant to these technologies?
3. If the government has provided funding, how much has been spent by the government on these trials? Can you provide NCT numbers?
4. Is the term in the proposed licenses to be life of patent or less than life of patent?
5. In working towards executing this license, has the NIH sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the "disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law"?
6. Considering the NIH has previously licensed CAR T technologies to Kite Pharma/Gilead, are the technologies identified in the current Federal Register notice related in any way to the previously executed licenses? (*List of previously noticed exclusive licenses on CAR T technologies to Kite Pharma follows below this email*)
7. Is there a Cooperative Research and Development Agreement associated with this technology?
8. Did the NIH previously post this technology in the Federal Register under "Government Inventions available for licensing"? And/or was it announced on any other platform that these technologies were available for licensing?
9. If not, how was it determined that Kite would enter into this proposed exclusive license, particularly considering the technology is currently under a provisional patent application?
10. Considering Kite/Gilead currently has CAR T therapy Yescarta (axicabtagene ciloleucel) on the market at a price of \$373,000, has/will the NIH seek license terms that will ensure the resultant therapy is available to patients on reasonable terms?

Thank you in advance for your assistance in this matter.

Sincerely,

Claire Cassedy

REL0000024100

Previously noticed exclusive licenses on CAR T technologies to Kite Pharma:

Prospective Grant of Exclusive License: Development of T Cell Receptors and Chimeric Antigen Receptors Into Therapeutics for Adoptive Transfer in Humans To Treat Cancer

<https://www.federalregister.gov/documents/2012/01/24/2012-1383/prospective-grant-of-exclusive-license-development-of-t-cell-receptors-and-chimeric-antigen>

Prospective Grant of Exclusive License: Development of T Cell Receptors for Adoptive Transfer in Humans to Treat Cancer

<https://www.federalregister.gov/documents/2014/03/25/2014-06412/prospective-grant-of-exclusive-license-development-of-t-cell-receptors-for-adoptive-transfer-in>

Prospective Grant of Exclusive License: Development of T Cell Receptors for Adoptive Transfer in Humans To Treat Cancer

<https://www.federalregister.gov/documents/2014/10/16/2014-24502/prospective-grant-of-exclusive-license-development-of-t-cell-receptors-for-adoptive-transfer-in>

Prospective Grant of Exclusive License: The Development of an Anti-CD19 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancers

<https://www.federalregister.gov/documents/2015/06/26/2015-15657/prospective-grant-of-exclusive-license-the-development-of-an-anti-cd19-chimeric-antigen-receptor-car>

Prospective Grant of Exclusive Patent License: Development of T Cell Receptors (TCRs) Targeting the KRAS G12D Mutation for the Treatment of Cancer

<https://www.federalregister.gov/documents/2016/08/17/2016-19549/prospective-grant-of-exclusive-patent-license-development-of-t-cell-receptors-tcrs-targeting-the>

Prospective Grant of Exclusive Patent License: Development of Anti-CD70 Chimeric Antigen Receptors for the Treatment of CD70 Expressing Cancers

<https://www.federalregister.gov/documents/2016/10/05/2016-24030/prospective-grant-of-exclusive-patent-license-development-of-anti-cd70-chimeric-antigen-receptors>

Prospective Grant of an Exclusive Patent License: The Development of an Anti-CD30 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer

<https://www.federalregister.gov/documents/2017/12/20/2017-27416/prospective-grant-of-an-exclusive-patent-license-the-development-of-an-anti-cd30-chimeric-antigen>

--
Claire Cassedy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

b5

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 4/5/2018 10:34:07 AM
To: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Wolinetz, Carrie (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1c655040d47346c7b04d7bc11a403ecb-wolinetzcd]; McGarey, Barbara (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f7a105a1715e459abe6d676d62d8f03b-mcgareyb]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Letter requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents on Exondys 51
Attachments: Exondys51-Eteplirs-en-patents-5April2018.pdf; Eteplirs-en-Exondys-51-cover-letter-5April2018.pdf

From: James Love [mailto:james.love@keionline.org]
Sent: Thursday, April 05, 2018 1:18 AM
To: secretary@hhs.gov
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Levinson, Dan R (OIG/IO) <dan.levinson@oig.hhs.gov>; Collins, Francis (NIH/OD) [E] <collinsf@od.nih.gov>; Kim Treanor <kim.treanor@keionline.org>; Andrew S. Goldman <andrew.goldman@keionline.org>; Manon Ress <manon.ress@keionline.org>
Subject: Letter requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents on Exondys 51

The Honorable Alex Azar
Secretary
Department of Health and Human Services
Via email: secretary@hhs.gov

Dear Secretary Azar,

Attached is a letter, signed by six organizations, asking for an investigation of and remedy to the failure of inventors to disclose several NIH grants in five patents on the drug Exondys 51. Also attached is a memo providing background on the failure to disclose the NIH grants in the specific patents.

We have requested a meeting with your staff to discuss this issue.

James Love
Knowledge Ecology International

cc::
The Honorable Daniel R. Levinson, Dan.Levinson@oig.hhs.gov;
Director Ann Hammersla, hammerslaa@mail.nih.gov
NIH Director Francis.Collins@nih.hhs.gov

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

REL0000024102

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 7/3/2019 4:34:37 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Pazman, Cecilia (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bf35741501e247d887acd224eaf9d679-pazmance]
Subject: Re: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

b5

From: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Date: Wednesday, July 3, 2019 at 12:30:31
To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>, "Pazman, Cecilia (NIH/NHLBI) [E]" <pazmance@nhlbi.nih.gov>
Subject: RE: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

Misha:

Thanks. b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, July 2, 2019 9:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Pazman, Cecilia (NIH/NHLBI) [E] <pazmance@nhlbi.nih.gov>
Subject: FW: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

Mark –
KEI letter with regards to my FR notice and my response.
Please comment.

Thank you,

Michael A. Shmilovich, Esq., CLP

REL0000024103



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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"Always be yourself....unless you can be a pirate... then; obviously, be a pirate"

From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Tuesday, July 2, 2019 1:31 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>
Subject: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

Dear Mr. Shmilovich:

Attached, please find Knowledge Ecology International's comments regarding the **Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063**, as well as the email correspondence referenced in the comments.

Sincerely,

Kathryn Ardizzone, Esq.
Knowledge Economy International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

REL0000024103

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/28/2017 5:37:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Bordine, Roger (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a44282b444584690bbbe471966f54f1f-bordinerw]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
CC: NIH FOIA [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e734b867d58f45e792d9fa7096aa146d-nihfoia]
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Mark – b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 28, 2017 13:17
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: NIH FOIA <nihfoia@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

b5

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Monday, August 28, 2017 9:52 AM
To: Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: NIH FOIA <nihfoia@od.nih.gov>; Deborah.Kassilke@nih.gov; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Roger – b5

b5

Thank you!!

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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REL0000024106

From: jamespackardlove@gmail.com [mailto:jamespackardlove@gmail.com] **On Behalf Of** Jamie Love
Sent: Monday, August 28, 2017 08:28
To: Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>
Cc: Claire Cassedy <claire.cassedy@keionline.org>; NIH FOIA <nihfoia@od.nih.gov>; Deborah.Kassilke@nih.gov; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Dear Roger Bordine,

I am attaching some correspondence I have had the NIH over the issue of CRADAs. When we respond to an NIH request for comments on an exclusive license, we often ask for the CRADA, if any, associated with the license. For example, recently we requested the CRADA associated with the miRecule CRADA, which involves a recent former NIH employee. Typically, as in the case of MiRecule, the NIH licensing officials refuses to give us a copy of the CRADA, claiming it is confidential. We both know that the CRADA document is in fact subject to FOIA, but FOIA takes a long time, can will not be processed before the comment period closes.

When we asked the Office of the Director for a list of all CRADA agreements earlier this year, we were told that the NIH would not provide such a list, because the information was in a computer database and the NIH was not required to create the list from the database under FOIA. We noted at the time that this would force us to FOIA all of the CRADAs, which we thought would be a waste of everyone's time, an opinion that you seemed to share.

Why doesn't the NIH do what some other federal agencies do and list the CRADAs, all of them, on the NIH web page, to enhance the transparency of the licensing and technology transfer operations?

In any event, please decide if the NIH wants to provide a list of the CRADAs or not, and if we have to sue to get copies if you won't in fact provide such a list.

The NIH knows full well the Congress, the press, academic researchers, taxpayer and patient advocacy groups all want to have more transparency of NIH technology transfer activities. The continual stonewalling of legitimate requests for public documents is inappropriate for an agency like the NIH that manages billions of taxpayer dollars to address important health issues, and where the pricing of NIH funded products is a major concern.

In the meantime, please provide KEI with a copy of the miRecule CRADA, and the list of the CRADAs, asap.

James Love
Knowledge Ecology International

Attached are portions of some previous correspondence with the NIH.

----- Forwarded message -----

From: NIH FOIA <nihfoia@od.nih.gov>
Date: Wed, Aug 16, 2017 at 5:15 PM
Subject: RE: Request FOIA Request Re: CRADAs Executed 2010-2017
To: Claire Cassedy <claire.cassedy@keionline.org>
Cc: NIH FOIA <nihfoia@od.nih.gov>

Good Afternoon,

REL0000024106

Thank you for your NIH FOIA request.

Upon reading your request, it appears as though you are asking for all CRADAs from the NIH between 2010-2017, and as it stands, that aspect of your request is too broad and would involve searching records from of all of the 27 institutes and centers at the NIH.

Searching for this many records, and the review efforts afterwards, would put an undue burden on Federal Government resources, as stipulated in the FOIA, and as such, requires you to narrow the scope of your request.

It is estimated that, within your requested timeframe, there would be hundreds of CRADAs across the NIH's institutes, and if you would like to submit a new/revised request detailing a smaller number of specifically named/individual CRADAs, you are more than welcome to request those records. If not, and you would rather request just a list of CRADAs and not the CRADA records themselves, you may do that instead.

Please let us know if you would like to withdraw this initial request in favor of submitting a new request for clarified/named records.

Thank you, and please let us know if you have any questions.

Roger Bordine

Program Assistant

Freedom of Information Office

National Institutes of Health

Building 31, Room 5B35

31 Center Drive

Bethesda, MD 20892

Phone: 301-496-5633

REL0000024106

Fax: 301-402-4541

Roger.bordine@nih.gov

----- Forwarded message -----

From: **James Love** <jamespackardlove@gmail.com>

Date: Thu, Jan 19, 2017 at 7:34 PM

Subject: Re: Your requests for information from NIH OTT

To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@od.nih.gov>

Cc: "Kassilke, Deborah (NIH/OD) [E]" <deborah.kassilke@nih.gov>, "claire.cassedy@keionline.org" <claire.cassedy@keionline.org>

We can't FOIA a database or require records be generated under FOIA. We can FOIA every CRADA, which is what we are going to be forced to do.

But if we knew what records were in the database, a query might save everyone a lot of time.

On Fri, Jan 20, 2017 at 1:07 AM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@od.nih.gov> wrote:

There is no "list" but we do have a database with CRADA and license information.

From: James Love [mailto:jamespackardlove@gmail.com]

Sent: Thursday, January 19, 2017 7:01 PM

To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>

Cc: claire.cassedy@keionline.org; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

Subject: Re: Your requests for information from NIH OTT

These are the types of data that make it hard to believe you don't have registry or list of the CRADAs.

<https://www.ott.nih.gov/tt-metrics/crada-metrics>

On Fri, Jan 20, 2017 at 12:56 AM, James Love <jamespackardlove@gmail.com> wrote:

Thank you.

We do note that the NIH is able to report the total number of CRADAs in any given year, and also that that number is quite a bit smaller than the number of CRADAs noticed in the federal register.

REL0000024106

For number of CRADAs, <https://www.ott.nih.gov/ott-statistics>

We are mostly interested in the Standard CRADAs.

We thought if the NIH could provide a count of the number of CRADAs, they must have a registry or list or database that lists the CRADAs, with the name of the CRADA partner and the purpose of the CRADA.

We were surprised when we were told that no such lists exist.

The CRADAs mentioned in the annual reports do not seem inclusive of all CRADAs in a given year.

For example:

In FY15, NIH Institutes executed 5,826 of these collaboration and transfer agreements, including 101 new Cooperative Research and Development Agreements (CRADAs).

I don't think there are 101 CRADAs listed in the annual report, or even the 73 for Standard CRADAs.

So, while the Annual report is useful and interesting, we still don't know who is getting the standard CRADAs.

Also, does the NIH issue exclusive licenses under the CRADAs that are not noticed in the federal register? We were told that the NIH practice was to not provide public notice and comment on all CRADAs and that public notice and comment is not available for all exclusive licenses from CRADAs.

Jamie

On Fri, Jan 20, 2017 at 12:26 AM, Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov> wrote:

Mr. Love –

Recently your office contact me and two other employees in my office with questions concerning royalty payments, the use of the Federal Registry in tracking NIH CRADAs, and a request for information on the process by which the NIH enters into a CRADA with an industry collaborator. I am aware that Mark Rohrbaugh (cc'd) spoke directly with Claire Cassidy to discuss many of the CRADA related process components including the use of

Federal Register notices and how IP is addressed in a CRADA. If you still have questions regarding the use of CRADAs at NIH, we can certainly schedule another call with you.

I confirmed that the NIH FOIA office is still working on a FOIA request for you concerning royalty payment information. They apologize for the delay, but the FOIA office is short staffed at this time and they are working diligently to hire and train new staff. We just last week brought in an Acting Director for the FOIA office, Katherine Uhl, who is on detail to us from the FDA. She is working diligently to keep the plates spinning and asked that I relay to you they are working on the request. Ms. Uhl invites you to contact her office for a status of your FOIA request if you so desire; that number is 301-496-5633.

I hope that you are aware that our annual reports and statistics can be found on our website in the "MEDIA Room" tab; they may be helpful to you.

Please let me know if you would like another call scheduled with Mark and me; we will gladly set something up.

Deb

Deborah Kassilke

Director, Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

E-Mail:

Deborah.Kassilke@nih.gov

Phone: 301-435-5294

Cell:

b6

From: Claire Cassedy [mailto:claire.cassedy@keionline.org]
Sent: Tuesday, August 15, 2017 11:38 AM
To: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>
Subject: Request FOIA Request Re: CRADAs Executed 2010-2017

Dear FOIA Officer,

Please find attached a Freedom of Information Act request from Knowledge Ecology International regarding Cooperative Research and Development Agreements executed by the NIH from 2010 to 2017. Thank you in advance for your attention to this request.

Sincerely,

Claire Cassedy

----- Forwarded message -----

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Date: Fri, Aug 18, 2017 at 10:34 AM
Subject: FW: miRecule CRADA
To: "jamespackardlove@gmail.com" <jamespackardlove@gmail.com>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutcha@nhlbi.nih.gov>, "Bailey, Brian (NIH/NHLBI) [E]" <bbailey@nhlbi.nih.gov>

Jamie – All scientific, business and financial information pertaining to the CRADA between MiRecule and NIDCD other than what has already been made public by either by publication, published patent applications or other public disclosures, is strictly confidential. As such, we cannot provide you with a copy of that agreement.

Regards,

Michael A. Shmilovich, Esq., CLP

REL0000024106

22 August 2017

James Packard Love
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

<http://keionline.org>

Work: +1.202.332.2670; Mobile: +1.202.361.3040

james.love@keionline.org

IN RE: 82 Fed. Reg. 36809 (August 7, 2017), "Prospective Grant of Exclusive Patent License: MicroRNA therapeutics for treating squamous cell carcinomas" to miRecule, Inc.

Dear Mr. Love:

....

Dr. Saleh will have direct participation in the research under his company's Cooperative Research and Development Agreement (CRADA) with the National Institute on Deafness and Other Communication Disorders (NIDCD) in order to advance the technology since a positive research outcome under the CRADA is one step closer to the development of a successful therapeutic to at least one squamous cell carcinoma. With respect to your request for various reports including CRADA documents, it is not consistent with our mission to create reports requested by the public and the proprietary content of the agreement governing the CRADA between the NIDCD is strictly confidential. In summary, the CRADA research plan sets forth a joint effort between miRecule and NIDCD to develop chemically modified mimic or mimetic microRNAs that are stable and less susceptible to nuclease degradation than previously identified microRNAs and that serve as therapeutics for cancer when delivered using tumor targeted nanoparticles. The CRADA will test these microRNAs in animal cancer models to evaluate their efficacy and the pharmaceutical properties of candidate formulations.

If your organization requests more documentation, such requests should be filed under the Freedom of Information Act. The webpage for the NIH FOIA Office provides more information on filing requests <http://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedominformation-act-office/submitting-foia-requests>.

Michael A. Shmilovich, Esq., CLP

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: Stevens, Ashley J [astevens@bu.edu]
Sent: 10/25/2016 1:49:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Fred Reinhart (fred@research.umass.edu) [fred@research.umass.edu]
Subject: RE: Publishing the updated drug study

The story of Gleevec is in one of the two books on it – are you aware of them? I can give you some dirt.

astevens@fipgllc.com

Subject: Re: Publishing the updated drug study

My office is working on a paper on kinase inhibitors starting with Gleevec as a breakthrough. Not focused on source of molecules.

Mark

On Oct 25, 2016, at 9:19 AM, Stevens, Ashley J <astevens@bu.edu> wrote:

b4

b4

Best regards,

Ashley

Ashley J. Stevens, D.Phil(Oxon), CLP, RTTP

<image001.jpg>

President

70 Yale Street, Suite 100
Winchester, MA 01890-2331

Tel: (781) 721-2670

Cell: **b6**
astevens@fipgllc.com

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 6/26/2018 3:02:48 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: A-257-2018 response to KEI

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 26, 2018 10:48 AM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: A-257-2018 response to KEI

b5

From: Berkley, Dale (NIH/OD) [E]
Sent: Monday, June 25, 2018 3:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: A-257-2018 response to KEI

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, June 25, 2018 9:56 AM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: Fwd: A-257-2018 response to KEI

b5

Sent from my iPhone

Begin forwarded message:

REL0000024109

From: "Greene, Jaime (NIH/NCI) [E]" <greenejaime@mail.nih.gov>
Date: June 25, 2018 at 9:43:53 AM EDT
To: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Cc: "Rodriguez, Richard (NIH/NCI) [E]" <richard.rodriguez@nih.gov>
Subject: FW: A-257-2018 response to KEI

Dear Mark,

Attached please find a response to KEI for your review.

The PD memo and FR notice can be found in the ELCG folder of Sharepoint:

<https://spweb.od.nih.gov/OTT/DTDT/ELCG/Forms/AllItems.aspx?RootFolder=%2FOTT%2FDTDT%2FELCG%2FApril%2025%2C%202018&FolderCTID=0x0120006450990D1683AD4896040FCDE1260FA6&View={844AB5DF-F7A9-4488-BC2E-FC9CB6F6C0E8}>

Please let me know if you have any concerns. I'd greatly appreciate a response by COB Wednesday, 6/27.

Thanks,

Jaime

Jaime Meredith Greene, M.S.
Senior Technology Transfer Manager
NCI Technology Transfer Center

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From: Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=NIH/NIAID/CN=MMOWATT]
Sent: 2/27/2017 3:57:48 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: FW: Question re: licensing government inventions

Hi Mark,

Writing to confirm that you will use the dial in below:

b6 participant code **b6**

Talk to you soon.

Thanks,

Mike

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Sunday, February 26, 2017 9:58 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Sayyid, Fatima (NIH/NIAID) [E] <fatima.sayyid@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <frisbies@otd.nci.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Subject: FW: Question re: licensing government inventions

Mark,

I've invited Fatima and Suzanne to join us on our call at 1100 Monday, so we'll need to use our conference line. I'll include it in the Outlook meeting invite, but here it is as well:

b6 participant code **b6**

Here's my draft response to NIAID policy/leg:

b5

b5

Talk to you Monday,

Mike

From: Selgrade, Sara (NIH/NIAID) [E]

Sent: Friday, February 24, 2017 11:05 AM

To: Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>

Cc: NIAID OCGR Leg <NIAIDOCGRLeg@mail.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <frisbies@otd.nci.nih.gov>; Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Harper, Jill (NIH/NIAID) [E] <JHarper@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>

Subject: Question re: licensing government inventions

Hi Mike,

Background

b5

Action Item

Would you be willing to provide a short bullet with some background on exclusive licensure of government inventions?

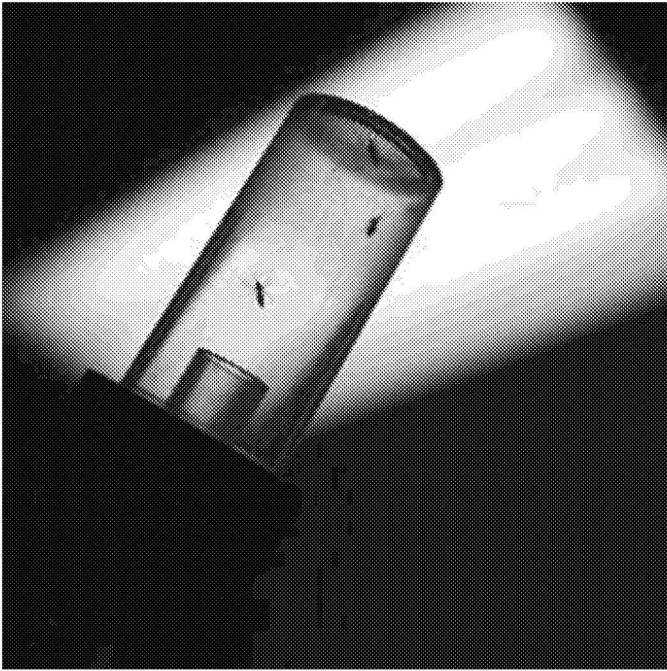
b5

I am happy to discuss further as needed.

Thanks very much for your help,
Sara

Lawmakers urge US Army not to issue exclusive license to Sanofi for a Zika vaccine

REL0000024111



John Moore/Getty Images Mosquitos caught for testing for

Zika and other mosquito-borne diseases.

By Ed Silverman @Pharmalot

February 22, 2017

Nearly a dozen members of Congress are urging the US Army not to issue an exclusive license to Sanofi Pasteur to develop a vaccine for the Zika virus over concerns the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

“In order to ensure that the investment made by taxpayers was worthwhile, it is critical that we ensure the vaccine to prevent against the Zika virus is accessible to anyone who requires it,” the lawmakers wrote on Wednesday in a letter to Robert Speer, the Acting Secretary of the Army.

But if the Army does proceed, the lawmakers implored Speer to issue a limited license and impose requirements that allow the federal government to intervene if the drug maker sets a price that “would make it accessible to millions of Americans who need access to a vaccine they paid to develop.” The letter was signed by 11 House Democrats.

The move comes after the military last December revealed plans to award the company a license to a pair of government patents. That followed months of mounting alarm among public health officials over the spread of Zika, the mosquito-borne virus that can cause birth defects. At the same time, there is speculation that the market for such a vaccine may become quite lucrative.

The government, however, has not disclosed specifics about the license. We do know that Sanofi Pasteur, which is one of the world’s biggest vaccine makers and a unit of the French pharmaceutical company, was awarded a \$43.2 million grant by the Biomedical Advanced Research and Development Authority and also has a co-development deal with the Walter Reed Army Institute of Research.

The lack of information prompted advocacy groups to complain to the Army, expressing concerns that the vaccine may be priced out of reach for many Americans, who helped fund the invention in the first place.

A Zika vaccine is being developed at warp speed, but will there be a market for it?

For instance, Knowledge Ecology International, a group that tracks access to medicines, asked the Army Medical Research and Materiel Command for information about the terms, such as how long the license would run, how much the government has spent, royalty rates, and pricing. The group made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit.

A KEI spokesman says request for information have not yet been fulfilled.

In comments filed last month to the US Army, Doctors Without Borders argued that an exclusive license will give Sanofi “a monopoly in the research, manufacturing and sale of the technology.” The advocacy group added that an exclusive license is no guarantee that all populations in need will be served and that Sanofi would be free to market to the most profitable markets.

We asked the US Army for comment and will update you accordingly.

A Sanofi Pasteur spokeswoman wrote us that the company is “well positioned” to clinically develop the vaccine and is “capable of making it available to those areas that need it most.” She also repeated what was told us two months ago — the vaccine maker has not yet created a specific commercial plan and could not say what price may eventually be charged or when the vaccine might become available. Late-stage testing has not begun. She did say the company expects to ask BARDA for more funding.

In a recent email exchange, Rachel Sachs, an associate professor at the Washington University School of Law, wrote us that “Sanofi may also gain additional collateral benefits associated with the vaccine that make [the] argument [by the advocacy groups] even stronger. The government may choose to stockpile doses of the vaccine, or purchase it in bulk for military service members overseas. Where the government is acting as purchaser, the ‘paying twice’ argument becomes clear: the government is paying for the clinical trials and may later be purchasing the vaccine at a monopoly price.”

Disclaimer: Any third-party material in this email has been shared under Fair Use provisions of U.S copyright law, without further verification of its accuracy/veracity. It does not necessarily represent my views nor those of NIAID, NIH, HHS, or the U.S. government.

From: Culhane, Ned (NIH/OD) [E] [/O=NIH/OU=NIEXCHANGE/CN=RECIPIENTS/CN=CULHANE]E]
Sent: 10/5/2016 9:17:56 PM
To: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIEXCHANGE/cn=Recipients/cn=hammerslaa]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Damianold]
Subject: FYI - Draft Pocan POTUS letter mentioning NIH/March-In

Hi Ann and Mark,

I saw the following HuffPost story about drug pricing and a draft letter to POTUS that Rep. Pocan is circulating about drug pricing. It offers three potential strategies to address the topic with NIH/Bayh-Dole listed first. 26 signers now with deadline Friday.

We've alerted OLPA leadership and going to give ASL a heads up at HHS. Our eyes are out for this and please let us know if you hear anything through your channels.

Best,
Ned

The President Can Act Against Drug Company Rip-Offs. These House Dems Explain.

10/05/2016 03:05 pm ET

Richard (RJ) Eskow Host, The Zero Hour; Sr. Fellow, Campaign for America's Future

Rep. Mark Pocan speaks with Richard Eskow on The Zero Hour

This week I spoke with Rep. Mark Pocan (D, WI) about an open letter to President Obama he is circulating to fellow members of Congress this week. It's an important letter, not only for its subject matter - it addresses our current crisis in runaway drug costs - but because it explains how the White House can address this issue without the need to pass legislation in the Republican-controlled House.

Most of us already know we've got a problem. A Kaiser survey released last week shows that 77 percent of Americans believe that "prescription drug costs are unreasonable."

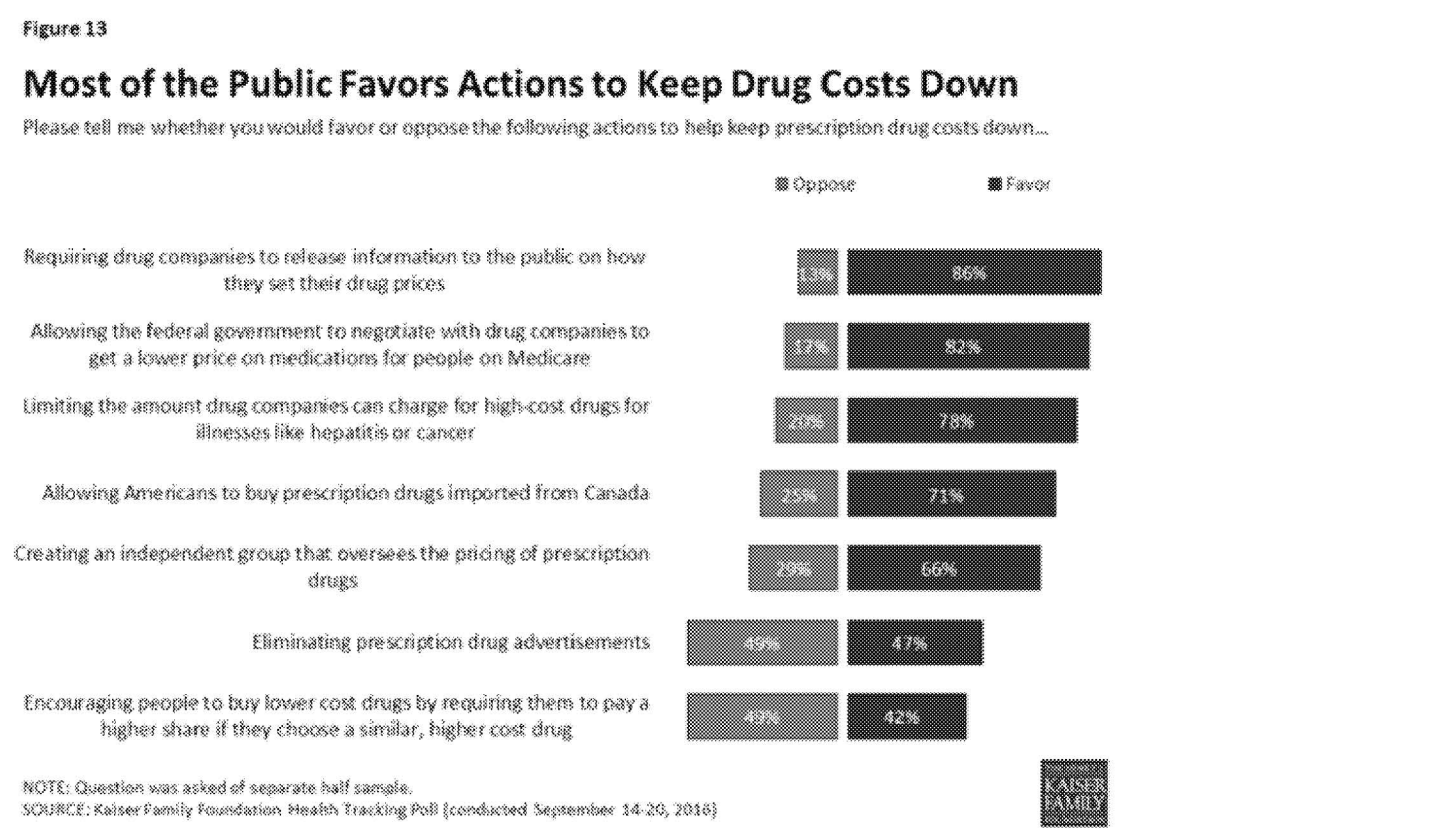
They're right. As the letter notes, Gilead Sciences recently set a price of \$84,000 for its 12-week course of Hepatitis C treatment - even though, as activist Annette Gaudino explained last August on The Zero Hour, it charges a fraction of that cost in other countries and still turns a profit. The letter also attacks the "price-gouging and anti-competitive behavior" of Mylan Pharmaceuticals, which jacked up the price of an EpiPen by nearly 500 percent over a five-year period.

Rep. Pocan's letter urges President Obama to "use executive action and take concrete steps" to address the drug cost crisis, and lists three tools that the president can use. The first is the Bayh-Dole Act, which gives the National Institutes of Health the power to ensure that medications that were developed at taxpayer expense are accessible to the public at affordable rates.

Next, the president can use the authority granted to the Secretary of Health and Human Services, under the Medicare Drug Act of 2003, to allow the importation of lower-cost drugs from other countries under certain conditions.

Lastly, the president to direct the Federal Trade Commission to stop drug companies’ monopolistic practices, especially when drug patent holders pay generic companies to delay lower-cost alternatives to market - a practice that is sometimes called “pay for delay.”

Most Americans already support strong action to rein in drug prices. The Kaiser survey showed, for example, that 82 percent of those polled support allowing the Federal government to negotiate drug prices and 71 percent support allowing Americans to purchase drugs imported for Canada.



The Pocan letter is supported by a number of activist groups, including Social Security Works, People’s Action, CREDO Action, and a number of other organizations. (See complete list below.)

A number of Democratic House members have signed Rep. Pocan’s letter. (No Republicans have signed it, which is telling: The Bayh-Dole Act was a bipartisan piece of legislation, which seems unimaginable today.) They are listed below.

If your Representative’s name isn’t on the list, they have until Friday to sign it. This would be a good time to call their office and suggest that they do.

Groups Supporting the letter: CREDO Action, Social Security Works, People Demanding Action, the Other 98%, Courage Campaign, Progressive Congress, Blue America, Public Citizen, Knowledge Ecology International (KEI), Daily Kos, Public Leadership Institute, People’s Action, and the Universities Allied for Essential Medicine.

(Note: I am affiliated with People's Action; Social Security Works sponsors The Zero Hour radio program on We Act Radio.)

House members who have signed the letter as of this writing:

*Lloyd Doggett
Jan Schakowsky
Keith Ellison
Raul Grijalva
Nydia M. Velázquez
Elijah E. Cummings
Jim McDermott
Alan Lowenthal
Jared Huffman
Luis Gutiérrez
Eleanor Holmes Norton
Sam Farr
Rosa DeLauro
Gwen S. Moore
John Conyers, Jr.
Earl Blumenauer
Barbara Lee
Maxine Waters
Steve Cohen
Brenda L. Lawrence
Michelle Lujan Grisham
John Yarmuth
Donna F. Edwards
Emanuel Cleaver
Peter Welch*

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 4/5/2018 4:42:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Letter requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents on Exondys 51
Attachments: Exondys51-Eteplirsen-patents-5April2018.pdf; Eteplirsen-Exondys-51-cover-letter-5April2018.pdf

From: James Love <james.love@keionline.org>
Sent: Thursday, April 05, 2018 1:18 AM
To: secretary@hhs.gov
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Levinson, Dan R (OIG/IO) <dan.levinson@oig.hhs.gov>; Collins, Francis (NIH/OD) [E] <collinsf@od.nih.gov>; Kim Treanor <kim.treanor@keionline.org>; Andrew S. Goldman <andrew.goldman@keionline.org>; Manon Ress <manon.ress@keionline.org>
Subject: Letter requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents on Exondys 51

The Honorable Alex Azar
Secretary
Department of Health and Human Services
Via email: secretary@hhs.gov

Dear Secretary Azar,

Attached is a letter, signed by six organizations, asking for an investigation of and remedy to the failure of inventors to disclose several NIH grants in five patents on the drug Exondys 51. Also attached is a memo providing background on the failure to disclose the NIH grants in the specific patents.

We have requested a meeting with your staff to discuss this issue.

James Love
Knowledge Ecology International

cc::
The Honorable Daniel R. Levinson, Dan.Levinson@oig.hhs.gov;
Director Ann Hammersla, hammerslaa@mail.nih.gov
NIH Director Francis.Collins@nih.hhs.gov

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

REL0000024114

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 7/3/2019 1:40:24 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Pazman, Cecilia (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bf35741501e247d887acd224eaf9d679-pazmance]
Subject: FW: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063
Attachments: MTTI-NIH license for Lutetium-177, 2 July 2019, KEI Comments.pdf; CassedyKEI_ShmilovichNIH_EmailsRE84FR28063.pdf; AbinderKEI_ShmilovichNIH_EmailsRE84FR28063.pdf; NIH to KEI re MTTI amendment 2 July 2019.docx

Mark –
KEI letter with regards to my FR notice and my response.
Please comment.

Thank you,

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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"Always be yourself...unless you can be a pirate... then; obviously, be a pirate"

From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Tuesday, July 2, 2019 1:31 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>
Subject: Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063

Dear Mr. Shmilovich:

Attached, please find Knowledge Ecology International's comments regarding the **Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 84 FR 28063**, as well as the email correspondence referenced in the comments.

Sincerely,

Kathryn Ardizzone, Esq.
Knowledge Economy International

REL0000024115

1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

July 2, 2019

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
31 Center Drive, Room 4A29, MSC2479
Bethesda, MD 20892-2479

Via email: shmilovm@mail.nih.gov

Re: 84 FR 28063, Prospective Grant of Exclusive Patent License: Lutetium-177
Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, to
Molecular Targeting Technologies, Inc. (MTTI), a Delaware corporation, with its principal place
of business in West Chester, Pennsylvania.

Dear Michael Shmilovich:

Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT)
are writing to provide comments on the prospective grant of an exclusive patent license for a
Lutetium-177 radiotherapeutics against somatostatin-receptor expressing neuroendocrine
tumors, to Molecular Targeting Technologies, Inc. (MTTI), a Delaware corporation.

On June 24, 2019, Claire Cassedy from KEI emailed you five questions about the proposed
license. You replied with answers to her questions on June 25, 2019. On June 26, 2019, Luis
Gil Abinader from KEI emailed you eight additional questions about the proposed license. You
replied with answers to his questions on June 27, 2019. Thank you again for your replies. Claire
Cassedy also emailed you on June 26, 2019 regarding whether the NIH has sought advice from
the Attorney General as is required under 40 U.S.C. § 559, we have yet to receive a reply to
that inquiry. We are providing a copy of these emails, including your replies, attached with our
comments.

**The NIH should comply with 40 U.S.C. § 559, which is not preempted by the Bayh-Dole
Act.**

At the appropriate time in the licensing process, we expect the NIH to obtain advice from the
Attorney General (as is required under 40 U.S.C. § 559) to determine if the “disposal to a private
interest would tend to create or maintain a situation inconsistent with antitrust law.”

The Bayh-Dole Act provides that “[n]othing in this chapter shall be deemed to convey to any
person immunity from civil or criminal liability, or to create any defenses to actions, under any
antitrust law[.]” 35 U.S.C. § 211.

The Bayh-Dole Act sets out the areas where the statute “shall take precedence over any other Act which would require a disposition of rights in subject inventions[,]” 35 U.S.C. § 210, and mentions 21 separate statutes, but does not include 40 U.S.C. § 559.

Intellectual property

With regards to the intellectual property to be licensed under the proposed agreement, the Federal Register notice 84 FR 28063 provides a list with one Patent Cooperation Treaty (PCT) international application and five additional patent documents.

The NIH Federal Register notice failed to explain whether the five patent documents (not including the PCT application) are issued patents or pending applications. The NIH notice also failed to explain where these five patent applications were filed, but we infer, based on their NIH reference number, that these applications were filed in the United States (2), China (1), the European Patent Office (1), and Japan (1). However, as we explain in more detail below and as you have confirmed to us in your email dated June 27, 2019, the proposed license also includes a national patent application filed in Singapore via the PCT procedure.

NIH reference number	Patent document	Filing date	Title
E-150-2016-0-US-01	62/333,427	5/9/2019	Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents.
E-150-2016-0-PCT-02	PCT/US2017/031696	5/9/2017	Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents.
E-150-2016-0-CN-03	201780029003X	11/9/2018	Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents.
E-150-2016-0-EP-04	17796666	11/12/2018	Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents.
E-150-2016-0-JP-05	2018-558662	11/8/2018	Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents.
E-150-2016-0-US-06	16/099,488	11/7/2018	Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents.

The field of use and geographical scope is described as follows in the Federal Register notice:

“The prospective patent license will be granted worldwide and limited to the extent that the above referenced patents or patent applications cover lutetium-177 radiotherapeutics for somatostatin-receptor expressing neuroendocrine tumors.”

In addition to the six patent documents listed above, the Federal Register notice has a catchall phrase stating that the intellectual property of the proposed exclusive license also includes “[...] all continuing U.S. and foreign patents/patent applications thereof [...]” As we interpret it, this phrase implies that all additional applications that entered their national phase via the PCT procedure PCT/US2017/031696 will be covered in the intellectual property scope of this license.

A search for the PCT application PCT/US2017/031696 using the WIPO database PatentScope returns one document, which has the publication number WO2017196806.¹ According to PatentScope, the PCT application PCT/US2017/031696 entered the national phase in the European Patent Office, Japan, the United States, but also in Singapore. The national number in Singapore according to PatentScope is 11201809982R. A search for the patent application number 11201809982R using the Intellectual Property Office of Singapore online search² returns one document, which has the United States of America as applicant and is titled *Chemical conjugates of evans blue derivatives and their use as radiotherapy and imaging agents*. This is the exact same title of the patent documents listed in the Federal Register notice.

In your June 27, 2019 email response to our questions you confirmed that the Singapore application 11201809982R will be covered in the proposed license and that it was not listed in the Federal Register notice because the filing number had not been reported to you on time. We thank you for confirming that this application will be covered in the license.

We also note that the NIH has the obligation to provide, when available, complete and accurate information about the intellectual property that it intends to license exclusively, including the national patent offices where relevant applications have been filed, in order to allow the public to fully evaluate and comment on whether the geographical scope of a proposed exclusive license complies with 35 U.S.C. § 209, or if the license will be consistent with the policies set out in the “United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy,” which states that “PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries.”

Molecular Targeting Technologies, Inc.

According to the Delaware Department of State Division of Corporations, MTTI was incorporated on December 20, 2001.³ MTTI’s website is <http://www.mtarget.com/SFNT.html>, which you confirmed to us in your June 27, 2019 email. According to its website, the mission of

¹ <https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2017196806>

² <https://www.ip2.sg/RPS/WP/CM/SearchSimpleP.aspx?SearchCategory=PT>

³ <https://icis.corp.delaware.gov/Ecorp/EntitySearch/NameSearch.aspx>

MTTI is to “translate novel radiopharmaceuticals for treatment and diagnosis of rare diseases.”⁴ The website describes four targets for therapeutics and diagnostics, which are “supported by published data and ongoing Phase I clinical trials.”⁵

One of the targets for therapeutics that Molecular Targeting Technologies lists on its website is “EBTATE (Lu-177-EB-DOTA-TATE)”, which is described as follows:

“EBTATE (Lu-177-EB-DOTA-TATE), a neuroendocrine tumor therapy (NET). EBTATE shows several-fold increase of blood half-life and enhanced tumor uptake over existing peptide receptor radionuclide therapy (PRRT).”⁶

MTTI also notes the following about its EBTATE target:

“First-in-human studies demonstrated a single low-dose EBTATE treatment appears to be safe and effective in the treatment of NEN. Demonstrated remarkably higher uptake and retention in neuroendocrine neoplasms. EBTATE could be effective with fewer, significantly lower doses than Lutathera®. An EBTATE suitable patient population includes metastatic, SSRTpositive NET patients.

“EBTATE is a peptide receptor radionuclide therapy (PRRT) for the treatment of somatostatin receptor positive gastroenteropancreatic neuroendocrine tumors. The drug binds to the somatostatin receptor expressing NET cells and destroys them. 80% NETs overexpress somatostatin receptors (particularly SSTR2).

“EBTATE was designed to overcome rapid clearing of Lutathera® by chemically incorporating an Evans Blue moiety in that framework. By increasing residence in albumin, EBTATE substantially lengthens the in vivo half-life increasing the probability of binding between drug and target. That enables fewer, lower doses of the radiotherapeutic.”⁷

MTTI also states on its website that the intellectual property related to MTTI’s EBTATE target is the PCT patent application PCT/US2017/054863, and that it holds a worldwide exclusive license over this patent application granted by the NIH.⁸

Previous NIH license to MTTI

On July 27, 2018, the NIH published the Federal Register notice [83 FR 35663](#), which also described a prospective exclusive license to Molecular Targeting Technologies (hereinafter “the

⁴ <http://www.mtarget.com/SFNT.html>

⁵ <http://www.mtarget.com/SFNT.html>

⁶ <http://www.mtarget.com/SFNT.html>

⁷ <http://www.mtarget.com/mm5/pdfs/pipeline/MTTI%20Asset%20EBTATE.pdf>

⁸ <http://www.mtarget.com/mm5/pdfs/pipeline/MTTI%20Asset%20EBTATE.pdf>

2018 exclusive license”).⁹ On August 27, 2018, KEI and UACT filed comments regarding the 2018 exclusive license, which are available here: <https://www.keionline.org/28697>.

The Federal Register notice for the 2018 exclusive license described one patent document:

“HHS Ref. E-150-2016-1-PCT-01, International Patent Application PCT/US2017/054863 filed October 3, 2017, entitled “Chemical Conjugates of Evans Blue Derivatives and Their Use As Radiotherapy And Imaging Agents.”

The PCT patent application listed in the Federal Register notice of the 2018 exclusive license¹⁰ has the same title as the applications listed in the Federal Register notice for the 2019 proposed license. The PCT application listed in the Federal Register notice of the 2018 exclusive license has two inventors, Xiaoyuan Chen and Orit Jacobson Weiss, who are the same two inventors listed in the PCT application described in the 2019 Federal Register notice. The geographical scope and the field of use of the 2018 exclusive license were described as follows:

“The prospective patent license will be granted worldwide and in a field of use not broader than radiotherapeutics for somatostatin-receptor expressing neuroendocrine tumors.”

A press release from Molecular Targeting Technologies dated October 8, 2018 and excerpted below suggests that the 2018 proposed license was indeed executed with this company:

“Molecular Targeting Technologies, Inc. (MTTI) announced today that the National Institute of Biomedical Imaging and Bioengineering (an Institute within the National Institutes of Health) granted MTTI an exclusive worldwide patent commercialization license. This patent estate invented by Drs. Xiaoyuan Chen and Orit Jacobson covers a radiotherapeutic (¹⁷⁷Lu-DOTA-EB-TATE (EBTATE)) with potential uses for treating Neuroendocrine Neoplasms (NENs).”¹¹

The 2019 Federal Register notice says that the proposed license would amend “an existing license.”¹² In your June 27, 2019 email you confirmed that the license in the Federal Register notice 83 FR 35663 has been executed and that this was the license that would be amended by the current Federal Register notice. You also confirmed in the same email that the 2018 exclusive license was executed. We thank you for clarifying that the license that would be amended is the 2018 exclusive license. We also note that the Federal Register notice could have been more specific and, for instance, cite the Federal Register notice of the license that would be amended.

⁹ <https://www.federalregister.gov/d/2018-16065>

¹⁰ <https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2019070236>

¹¹ <http://www.mtarget.com/mm5/pdfs/2018Oct8NETNIH.pdf>

¹² <https://www.federalregister.gov/d/2019-12708>

We asked you how the proposed license would amend the 2018 exclusive license. Our question on this issue and your answer in your June 27, 2019 email are copied below.

“How will the exclusive license proposed in the Federal Register notice 84 FR 28063 amend the previous license described in the Federal Register notice 83 FR 35663?”

“The amendment adds the IP rights listed in this FR notice but narrows the field of use of the license to ¹⁷⁷Lu radiotherapeutics. If you look through the claims of the published PCT there is a list of other potential radionuclides that can be used therapeutically.”

We asked you what is the rationale for granting additional exclusive rights to a company that presumably has outstanding obligations under a previous license. Our question and your June 27, 2019 response are copied below.

“What is the rationale for granting additional exclusive rights to a company that presumably has outstanding obligations under a previous license?”

“The company has no outstanding obligations. The company and NIH discussed that the instant patent rights should be included to complete the patent portfolio licensed by the company so long as it is constrained by field of use.”

177 Lu-DOTA-EB-TATE therapeutics

The Federal Register notice provides the following description of the invention:

“The invention pertains to a radiotherapeutic against neuroendocrine tumors that express somatostatin receptor. Radionuclide therapies directed against tumors that express somatostatin receptors (SSTRs) have proven effective for the treatment of advanced, low- to intermediate-grade neuroendocrine tumors. The subject radiotherapeutic covered by the subject patent estate includes a somatostatin (SST) peptide derivative like octreotate (TATE), conjugated to an Evans Blue (EB) analog, and further chelated via DOTA to therapeutic radionuclide. The EB analog reversibly binds to circulating serum albumin and improves the pharmacokinetics of SST peptide derivatives and reduce peptide-receptor radionuclide therapy toxicity. EB analog conjugated to octreotate (EB-DOTATATE) has been shown by the inventors to provide reversible albumin binding in vivo and extended half-life in circulation. When EB-TATE is slowly released into the tumor microenvironment, tumor uptake and internalization into SSTR positive tumors resulted in delivery of radioactive particles and tumor cell killing. EB-TATE displayed significantly more favorable pharmacokinetics than TATE alone by achieving higher tumor to non-tumor penetration as evidenced by positron emission tomography.”

A clinicaltrials.gov search for the term “DOTA-EB-TATE” returns two phase I clinical trials, NCT03308682¹³ and NCT03478358,¹⁴ both related to neuroendocrine tumors. These trials were co-sponsored by the Peking Union Medical College Hospital and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), according to clinicaltrials.gov.

We asked you whether these trials were related to the proposed license, and you replied that they were not. Our exchange on this question, including your answer, is copied below.

“A clinicaltrials.gov search for the term “DOTA-EB-TATE” returns two phase I clinical trials, NCT03308682 and NCT03478358, both related to neuroendocrine tumors. These trials were co-sponsored by the Peking Union Medical College Hospital and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), according to clinicaltrials.gov. Are these trials related to the proposed exclusive license?”

“Not related.”

However, a paper published November 2018 in the Journal of Nuclear Medicine by Xiaoyuan Chen, one of the inventors in the PCT application covered in the proposed license, and eight other co-authors reported the results of the clinical trial NCT03308682.¹⁵ That paper describes the clinical trial NCT03308682 as a “noncontrolled, nonrandomized, nonblinded first-in-humans study” that explored “the safety and dosimetry of a long-acting radiolabeled somatostatin analog, 177Lu-1, 4, 7, 10-tetra-azacyclododecane-1, 4, 7, 10-tetraacetic acid-Evans blue-octreotate (177LuDOTA-EB-TATE).”¹⁶

The paper co-authored by Xiaoyuan Chen suggests that in “a recently finished phase III clinical trial, a treatment with 177Lu-DOTATATE resulted in markedly longer progression-free survival and a significantly higher response rate than high-dose octreotide long-acting repeatable (LAR) among patients with advanced midgut NET.”¹⁷ The paper further explains that “the promising results from this trial” led to the approval of Lutathera by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA).¹⁸ According to the FDA approval letter dated January 26, 2018, Lutathera is indicated “for the treatment of somatostatin receptor positive GEP-NETs including foregut, midgut, and hindgut neuroendocrine tumors in adults.”¹⁹ The original FDA NDA applicant was Advanced Accelerator Applications USA, Inc.²⁰

¹³ <https://clinicaltrials.gov/ct2/show/NCT03308682>

¹⁴ <https://clinicaltrials.gov/ct2/show/NCT03478358>

¹⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225536/pdf/1699.pdf>

¹⁶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225536/pdf/1699.pdf>

¹⁷ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225536/pdf/1699.pdf>

¹⁸ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225536/pdf/1699.pdf>

¹⁹ https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2018/208700Orig1s000ltr.pdf

²⁰ https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2018/208700Orig1s000ltr.pdf

The NCT03308682 trial exposed five patients to 177Lu-DOTA-EB-TATE and compared them with three patients that received Lutathera (177Lu-DOTATATE).²¹ The conclusion of this clinical trial, as reported by Xiaoyuan Chen et al. in the Journal of Nuclear Medicine, was the following:

“By introducing an albumin-binding moiety, 177Lu-DOTA-EBTATE showed significantly higher NET uptake and retention over 177Lu-DOTATATE. This first-in-humans study demonstrates that 177Lu-DOTA-EB-TATE is safe and well tolerated in NET patients.”²²

We recall that Molecular Targeting Technologies, the prospective licensee in this case, states on their website that: “EBTATE was designed to overcome rapid clearing of Lutathera® by chemically incorporating an Evans Blue moiety in that framework. By increasing residence in albumin, EBTATE substantially lengthens the in vivo half-life increasing the probability of binding between drug and target. That enables fewer, lower doses of the radiotherapeutic.”²³

We also recall that the Federal Register notice 84 FR 28063 states the following: “EB-TATE displayed significantly more favorable pharmacokinetics than TATE alone by achieving higher tumor to non-tumor penetration as evidenced by positron emission tomography.”

In summary, based on our own research and information available in the Federal Register notice, 177Lu-DOTA-EBTATE potentially has more favorable pharmacokinetics compared to 177Lu-DOTATATE, a therapy for neuroendocrine tumors recently approved by the FDA. We asked you whether this was correct. Our exchange on this question is copied below.

KEI: “Based on our own research, our understanding is that the invention covered in the proposed license, 177Lu-DOTA-EBTATE, has more favorable pharmacokinetics compared to 177Lu-DOTATATE, a therapy for neuroendocrine tumors recently approved by the FDA and marketed under the brand name Lutathera. Is this correct?”

NIH: “We hope so as does the company; however, this remains to be determined through controlled clinical trials.”

NIH RePORTER project number EB000073

A NIH RePORTER search for “NCT03308682” in the “ClinicalTrials.gov ID” field returns one project identified with the number EB000073 and titled *Laboratory of molecular imaging and nanomedicine*. This project received \$27,897,781 in funding over the course of 9 years. The principal investigator in this project was Xiaoyuan Chen, who is also one of the inventors in the PCT application PCT/US2017/031696. The table below provides information on the total cost by year of the project number EB000073, based on data retrieved from the NIH RePORTER.

²¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225536/pdf/1699.pdf>

²² <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225536/pdf/1699.pdf>

²³ <http://www.mtarget.com/mm5/pdfs/pipeline/MTTI%20Asset%20EBTATE.pdf>

Project	Project Title	Contact PI/ Project Leader	FY	Admin IC	Total Cost
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2018	NIBIB	\$3,716,858
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2017	NIBIB	\$2,628,647
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2016	NIBIB	\$4,443,729
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2015	NIBIB	\$3,090,898
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2014	NIBIB	\$3,046,083
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2013	NIBIB	\$2,833,485
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2012	NIBIB	\$2,930,853
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2011	NIBIB	\$3,139,811
EB000073	LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE	CHEN, XIAOYUAN	2010	NIBIB	\$2,067,417

In the event that the NIH decides to grant this exclusive license, we ask that the following safeguards be placed on the license.

1. **Price discrimination.** Any drug or other medical technology using the patented invention should be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method. This is a modest safeguard.
2. **Low and middle income countries.** The exclusive license should not extend to countries with a per capita income less than 30 percent of the United States, in order to ensure that the patents do not lead to restricted and unequal access in developing countries. If the NIH rejects this suggestion, it needs to provide something that will give effect to the policy objective in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states the following: "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

3. **Global registration and affordability.** The license should require Molecular Targeting Technologies, Inc, to disclose the steps it will take to enable the timely registration and availability of the drug or other medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the World Health Organization (WHO), either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so.
4. **Medicines Patent Pool.** The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the drug or other medical technology from competitive suppliers, including technology transfer, in developing countries, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the drug or other medical technology.
5. **Years of exclusivity.** We propose the license reduce the years of exclusivity when revenues are large. The NIH has many options, including by providing an option for non-exclusive licensing, such as was done in the ddi case. We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. For example, the period of exclusivity in the license could be reduced by one year for every \$500 million in global cumulative revenue after the first one billion in global sales. This request is consistent with the statutory requirements of 35 U.S.C. § 209, which requires that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.”
6. **Transparency of R&D outlays.** The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.” Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to practical application.

Sincerely,

Kathryn Ardizzone and Luis Gil Abinader on behalf of:

Knowledge Ecology International (KEI)
Union for Affordable Cancer Treatment (UACT)

And in their personal capacity,

James Love
Manon Ress
Luis Gil Abinader



Claire Cassedy <clairepcassedy@gmail.com>

Inquiry regarding 84 FR 28063 Doc 2019-12708 - Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors

Claire Cassedy <claire.cassedy@keionline.org>

Wed, Jun 26, 2019 at 10:34 AM

To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>

Dear Mr. Shmilovich,

Thank you very much for your prompt reply. I have one more question regarding this proposed license:

-In working towards executing this license, has the NIH sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the "disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law"?

I appreciate all your assistance on these inquiries.

--

Claire Cassedy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

On Tue, Jun 25, 2019 at 11:28 AM Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov> wrote:

Dear Claire --

1. At what stage of development are the inventions listed?

Pre-clinical, early stage.

2. Has the government funded any clinical trials relevant to these technologies?

No

3. If the government has provided funding, how much has been spent by the government on these trials?
Can you provide NCT numbers?

N/A

4. How many years of exclusivity have been offered in this agreement, and what will the royalty rate be?

Royalty rates and terms of the license have yet to be negotiated but are, in general, confidential.

5. Regarding the company to receive the licenses, Molecular Targeting Technologies, Inc. are any former NIH employees associated with the company?

I'm not aware of any

From: Claire Cassedy <claire.cassedy@keionline.org>

Sent: Monday, June 24, 2019 12:32

To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>

Subject: Inquiry regarding 84 FR 28063 Doc 2019-12708 - Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors

Dear Mr. Shmilovich,

I am writing in reference to the Federal Register notice (84 FR 28063 Doc 2019-12708) regarding, "Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors," for which you are listed as the contact for inquiries. I was hoping you could provide me with some further information regarding the status of the technologies.

1. At what stage of development are the inventions listed?
2. Has the government funded any clinical trials relevant to these technologies?
3. If the government has provided funding, how much has been spent by the government on these trials?
Can you provide NCT numbers?
4. How many years of exclusivity have been offered in this agreement, and what will the royalty rate be?
5. Regarding the company to receive the licenses, Molecular Targeting Technologies, Inc. are any former NIH employees associated with the company?

Thank you in advance for your assistance in this matter.

Best Regards,
Claire Cassedy

--

Claire Cassedy

Knowledge Ecology International

1621 Connecticut Avenue NW

Suite 500

Washington, DC 20009

Tel.: 1.202.332.2670



Claire Cassedy <clairepcassedy@gmail.com>

Additional inquiry regarding 84 FR 28063 Doc 2019-12708, "Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors"

Luis Gil Abinader <luis.gil.abinader@keionline.org>

Thu, Jun 27, 2019 at 9:40 AM

To: Jamie Love <james.love@keionline.org>, "claire.cassedy" <claire.cassedy@keionline.org>

Cc: Kathryn Ardizzone <kathryn.ardizzone@keionline.org>, Laurel Boman <laurel.boman@keionline.org>

----- Forwarded message -----

From: **Shmilovich, Michael (NIH/NHLBI) [E]** <michael.shmilovich@nih.gov>

Date: Thu, Jun 27, 2019 at 9:32 AM

Subject: RE: Additional inquiry regarding 84 FR 28063 Doc 2019-12708, "Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors"

To: Luis Gil Abinader <luis.gil.abinader@keionline.org>

Dear Mr. Abinader— With regards to your questions:

Dear Mr. Abinader – thank you for your email. The answers to your questions are as follows:

1. Does the license includes the Singapore patent application 11201809982R, which entered the national phase via the PCT procedure PCT/US2017/031696?

Yes, the Singapore application filing number wasn't reported to us in time for the FR notice but that application will be included.

2. Is <http://www.mtarget.com/SFNT.html> the website of the prospective licensee?

Yes

3. The Federal Register notice 84 FR 28063 states that the NIH is contemplating amending "an existing license". Is the "existing license" the prospective exclusive license described in the Federal Register notice 83 FR 35663, published on July 27, 2018?

Yes, this will be an amendment to that now executed license.

4. Was the license proposed in the Federal Register notice 83 FR 35663 executed?

Yes

5. How will the exclusive license proposed in the Federal Register notice 84 FR 28063 amend the previous license described in the Federal Register notice 83 FR 35663?

The amendment adds the IP rights listed in this FR notice but narrows the field of use of the license to ¹⁷⁷Lu radiotherapeutics. If you look through the claims of the published PCT there is a list of other potential radionuclides that can be used therapeutically.

6. What is the rationale for granting additional exclusive rights to a company that presumably has outstanding obligations under a previous license?

The company has no outstanding obligations. The company and NIH discussed that the instant patent rights should be included to complete the patent portfolio licensed by the company so long as it is constrained by field of use.

7. A clinicaltrials.gov search for the term "DOTA-EB-TATE" returns two phase I clinical trials, NCT03308682 and NCT03478358, both related to neuroendocrine tumors. These trials were co-sponsored by the Peking Union Medical College Hospital and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), according to clinicaltrials.gov. Are these trials related to the proposed exclusive license?

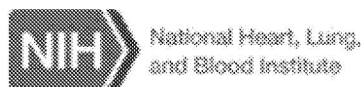
Not related.

8. Based on our own research, our understanding is that the invention covered in the proposed license, ¹⁷⁷Lu-DOTA-EBTATE, has more favorable pharmacokinetics compared to ¹⁷⁷Lu-DOTATATE, a therapy for neuroendocrine tumors recently approved by the FDA and marketed under the brand name Lutathera. Is this correct?

We hope so as does the company; however, this remains to be determined through controlled clinical trials.

Regards,

Michael A. Shmilovich, Esq., CLP



Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019

shmilovm@mail.nih.gov

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"Always be yourself....unless you can be a pyrate... then, obviously, be a pyrate"

[Quoted text hidden]

b5

From: Frisbie, Suzanne (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C402740CEAAD4D4F97A8C28F16FBB349-FRISBIES]
Sent: 6/7/2018 4:45:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]
Subject: RE: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

Hi Mark and Mike,

b5

Suzanne

From: Soukas, Peter (NIH/NIAID) [E]
Sent: Thursday, June 07, 2018 12:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <Suzanne.Frisbie@nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <RWILLIAMS@niaid.nih.gov>
Subject: FW: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

Dear Mark and Mike,

I just received this email from KEI. b5

b5

b5

Thanks.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: James Love <james.love@keionline.org>
Sent: Thursday, June 7, 2018 12:16 PM
To: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>
Cc: Manon Ress <manon.ress@keionline.org>; luis.gil.abinader@keionline.org; Claire Cassedy <claire.cassedy@keionline.org>
Subject: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

Peter Soukas, Technology Transfer and Patent Specialist,
Technology Transfer and Intellectual Property Office,
National Institute of Allergy and Infectious Diseases,
National Institutes of Health,
Email:

REL0000024116

ps193c@nih.gov

Dear Peter Soukas,

We are responding to the request for comments on the Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines, to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

*

We note the "

The Licensed Territory may be limited to Europe, China, South Korea, Japan, India, Australia and New Zealand.

"

We oppose granting an exclusive license in the Territory of India, a country with an average income of \$1,670 in 2016, according to the World Bank. India is also a possible source of the vaccine for other developing countries, so the granting of an exclusive license may result in broader restrictions on access.

Sincerely,

James Love
KEI

*

<https://www.federalregister.gov/documents/2018/05/25/2018-11258/prospective-grant-of-exclusive-license-production-of-monovalent-live-attenuated-zika-vaccines-and>

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/20/2018 6:53:29 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: NIH to KEI re Inversago T1D 20Aug2018.docx
Attachments: NIH to KEI re Inversago T1D 20Aug2018.docx

Mark and Alan –

Enclosed for your comment. Please feel free to share with anyone else you feel might have useful input.

b5

b5

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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"Always be yourself...unless you can be a pirate... then; obviously, be a pirate"

REL0000024117

b5

b5

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 6/26/2018 3:57:41 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertson]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion
Attachments: 9--RESPONSE in Opposition re 5--6.25.2018.pdf

Attached is KEI's response to our motion to dismiss, just for your information, no action necessary. Please distribute to any others in management who have an interest or need to know.

b5

b5

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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REL0000024121

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND (SOUTHERN DIVISION)

*

KNOWLEDGE ECOLOGY INTERNATIONAL,

*

Plaintiff

*

v.

*

NATIONAL INSTITUTES OF HEALTH, *et al.*,

*

Defendants

*

* * * * *

**PLAINTIFF'S MEMORANDUM IN
OPPOSITION TO DEFENDANTS' MOTION TO DISMISS**

Plaintiff, Knowledge Ecology International ("KEI"), by and through its undersigned attorneys, hereby submits this Memorandum in Opposition to the Motion to Dismiss (Doc. No. 5) filed by Defendants National Institutes of Health ("NIH") and Francis Collins in his official capacity with NIH ("Mr. Collins" or, collectively, "NIH"), and National Cancer Institute ("NCI") and David Lambertson in his official capacity with NCI ("Mr. Lambertson" or collectively "NCI", and, collectively with all of the above, "Defendants"); and, as reasons therefore, states:

INTRODUCTION

In January 2018, Defendants rejected Plaintiff's substantive recommendations for public interest safeguards and declared that they would grant an exclusive license of critical CAR T cancer treatment technology to a large pharmaceutical corporation with a history of excessive pricing, including on one of

the only other two CAR T cancer treatments currently on the market. In February 2018, Defendants announced that they would proceed without providing Plaintiff the opportunity to set forth the arguments of why it merited an appeal under the statutes and regulations of the Bayh Dole Act.

Additionally, Defendants admitted to failing to abide by the black letter obligations of the Federal Property and Administrative Services Act with regard to seeking and obtaining antitrust advice from the Attorney General prior to disposing of federal property, including patents, to private interests.

As set forth in detail in the Complaint, both of these sets of actions constitute statutory and/or regulatory issues in their own right, in addition to being violations of relevant sections of the Administrative Procedure Act.

In response to KEI's Complaint attempting to call attention to their illegal actions, Defendants attempt to avoid these issues entirely by convincing the Court that KEI lacks standing to bring Defendants to task.

In so doing, Defendants erroneously insist that this Court is bound by a "functional equivalency" test that has yet to be accepted by the Fourth Circuit and that this Court must adhere to a rigid interpretation of the law of associational standing that the Supreme Court has never embraced and where other jurisdictions have shied away from such a formulaic approach. Furthermore, KEI can establish organizational standing because it has diverted a substantial amount of resources toward redressing the issues asserted in the Complaint, to the detriment of KEI's mission.

Contrary to Defendants' assertions, KEI's Complaint laid out a clear set of facts showing that it and the consumers, patients and taxpayers that it represents were injured by Defendants' unlawful acts; therefore, as discussed more fully *infra*, KEI's standing is sufficiently established and Defendants should be required to answer to this Court for their improper actions.

ARGUMENT

All that a plaintiff must allege in order to establish standing is that it has: "(1) suffered an injury-in-fact, (2) that is fairly traceable to the challenged conduct of the defendant, and (3) that is likely to be redressed by a favorable judicial decision." *Hutton v. Nat'l Bd. of Examiners in Optometry, Inc.*, No. 17-1506, 2018 WL 2927626, at *4 (4th Cir. June 12, 2018) (quoting *Spokeo, Inc. v. Robins*, — U.S. —, 136 S.Ct. 1540, 1547, 194 L.Ed.2d 635 (2016)). This Court recently instructed that "[i]njury-in-fact is not Mount Everest." *District of Columbia v. Trump*, 291 F.Supp.3d at 738 (quoting *Danvers Motor Co. v. Ford Motor Co.*, 432 F.3d 286, 294 (3d Cir. 2005) (Alito, J.)).

"At the pleading stage, general factual allegations of injury resulting from the defendant's conduct may suffice, [since] on a motion to dismiss [the court] presum[es] that general allegations embrace those specific facts that are necessary to support the claim." *Lujan*, 504 U.S. at 561, 112 S.Ct. 2130 (citation and quotation marks omitted).

I. KEI's Has Sufficient Indicia-of-Membership to Have Associational Standing Because Patients, Taxpayers, and Consumers Control KEI's Functions, Serve on KEI's Leadership, and Finance KEI's Activities.

In support of their argument that Plaintiff lacks standing, Defendants rely in large part upon their assertion that KEI “apparently has no members;” however, as Defendants later acknowledge, the law is clear that associational standing is not limited to traditional membership organizations. (*Compare* Doc. No. 5-1, p.10 with *Hunt v. Washington Apple Advertising Comm’n*, 432 U.S. 333, 344 (1977).)

The proper test, as the Supreme Court stated in *Hunt* is whether the persons whose interests were affected “possessed all of the indicia of membership in an organization,” and the functions performed by the organization, which included engaging in “advertising, market research and analysis, public education campaigns, and scientific research” in support of the Washington apple industry. *Id.* at 334.

Following *Hunt*, courts have determined that organizations may have associational standing without members if the organization is the functional equivalent of a member organization. *Heap v. Carter*, 112 F.Supp.3d 402, 418-19 (E.D. Va. 2015) (citing *Washington Legal Found. V. Leavitt*, 477 F.Supp.2d 202, 208 (D.D.C. 2007) (adopting the ruling in *Hunt* as a rigid test: the organization “(1) serves a specialized segment of the community; (2) represents individuals that have all the indicia of membership, including (i) electing the entity’s leadership, (ii) serving in the entity, and (iii) financing the entity’s activities, and (3) its fortunes are tied closely to those of its constituency.”)

A. KEI Meets the Functional Equivalency Test to Establish Associational standing.

The record demonstrates that KEI is a well-respected nongovernmental organization: (i) with a long track record of working for a constituency of consumers, patients and taxpayers on issues relating to intellectual property and access to affordable medicines; (ii) that has leadership, including a Board of Directors, a Nobel prize-winning Board of Advisers, and staff, that are directly affected by such issues and who guide the work of KEI; and (iii) that receives feedback and guidance from its constituency via its IP-Health listserv and through regular meetings, and receives individual donations from its constituency.

Attempting to undermine these clear indicia of standing, Defendants assert rather flippantly that KEI “apparently often opines on the new costs of new medical technologies,” and that KEI lacks associational standing because it has not shown that the constituency that KEI “purports to ‘represent’ ... (i) elects KEI’s leadership (or even of what KEI’s leadership is comprised), (ii) serves activities and goings-on (whatever they may be), or (iii) finances KEI’s budget.” Defendants’ Memorandum in Support of Motion to Dismiss, p.11, 13. In fact, KEI meets this functional equivalency test for the reasons provided in the Complaint, and as further explained in the Declaration of James Packard Love (“Love Declaration”).

i. KEI has a long history of representing patients and consumers on issues at the intersection of intellectual property and access to affordable medicines.

As mentioned in the Complaint, KEI is an award-winning non-profit organization with a lengthy, well-established track record of public service on issues relating to intellectual property and public health. Complaint, ¶5. The organization

was founded by Director James Packard Love in 2006 upon a prestigious MacArthur Award for Creative & Effective Institutions, based largely upon Mr. Love's work at predecessor organizations the Consumer Project on Technology and the Taxpayer Assets Project. Love Declaration ¶13. At those organizations, Love did groundbreaking work in the field of access to medicines, including successfully negotiating a \$1/day price for a three-drug combination treatment for HIV/AIDS with the generic drug manufacturer Cipla in 2001 that is credited with making the medicines affordable for countries in Africa and other developing countries that were suffering through a horrendous crisis with the disease. Love Declaration, ¶19; *See also* Sarah Boseley, *Big Pharma's Worst Nightmare*, The Guardian, Jan. 26, 2016 (available at: <https://www.theguardian.com/society/2016/jan/26/big-pharmas-worst-nightmare>). Mr. Love is an internationally recognized expert in the field of access to medicines and intellectual property rights, and, through KEI or its predecessor organizations, has authored important materials for the World Health Organization ("WHO"), World Intellectual Property Organization ("WIPO"), UNITAID, and as an expert witness in compulsory licensing cases in South Africa and India. Love Declaration, ¶¶ 20-27.

As mentioned in the Complaint, under Mr. Love's direction KEI routinely works on issues pertaining to the licensing of federally-funded medical technologies. Complaint ¶5. Since 2015, Mr. Love and KEI have filed comments on over thirty proposed exclusive patent licenses, with most comments consistently focusing on "(1) standards to protect against excessive or discriminatory pricing, (2) provisions

to protect or expand access in developing countries, and (3) requests for transparency of R&D investments, prices and revenues related to the commercialization of products using the inventions.” Love Declaration, ¶38-39.

Mr. Love and KEI have a specific and well-documented interest and expertise in issues regarding the expansion of access to affordable treatments for cancer and rare diseases. KEI is one of six partner organizations of the Union for Affordable Cancer Treatment, and is in official relations with the World Health Organization, working in collaboration to expand access to, and the affordability of, cancer treatments. *Id.* ¶¶61-62. Mr. Love has been asked to advise U.S. agencies and member states on issues relating to the pricing and affordability of drugs, vaccines, and new gene- and cell-based treatments such as the CAR T therapy at issue in this case, and has been invited to present at various WHO-sponsored meetings and roundtables on noncommunicable diseases (“NCDs”). *Id.* ¶64. KEI has special accreditation to participate in a series of meetings and negotiations relating to the United Nations High-Level Meetings on NCDs. *Id.* KEI is a member of the Transatlantic Consumer Dialogue (TACD), a coalition of sixty consumer groups in the United States and Europe, and Mr. Love is the elected U.S. co-chair of the TACD policy committee on intellectual property. *Id.*, ¶60.

In all meetings in these or other fora, KEI and Mr. Love are expected to represent the interests of the public as patients or persons who pay for health insurance. *Id.*

ii. KEI's leadership and staff is directly affected by the underlying issues of the high prices of cancer medicines, and KEI's Board of Directors and Board of Advisers Guide the Work of KEI.

The high price of cancer medicines directly affects KEI's staff, including both Mr. Love himself, who was treated for squamous cell carcinoma skin cancer, and Mr. Love's wife, Manon Ress, KEI's Director of Information Society Projects, who was diagnosed in 2010 with HER2+ breast cancer. Love Declaration, ¶¶ 29, 31. Ms. Ress is currently treated with an expensive, NIH-funded medicine sold by Roche as Kadcyla, for stage 4 HER2+ breast cancer patients. *Id.* Ms. Ress lost her mother to breast cancer in 2007, and has a sister who has been treated for breast cancer. *Id.* ¶ 30. Mr. Love has additionally lost a father to cancer, and has several other family members that currently have cancer, including his mother and two brothers. *Id.* ¶ 32. One brother "has been diagnosed and treated for diffuse large B cell lymphoma (DLBCL), one of the indications in the proposed license [by Defendants] to Gilead" of the CAR-T patents. *Id.*

In lieu of members, KEI has a Board of Directors, which manages the affairs of KEI as provided in Article 3 of the Bylaws, and a Board of Advisors that guide the direction of KEI's work. *Id.* ¶¶ 3-6. The Board of Directors currently consists of academics, established public advocates and attorneys, patients, consumers, and activists on issues regarding access to affordable medicines. *Id.* The Board of Directors elects the executive director of KEI and other officers at each annual meeting, per Article 5 of the Bylaws. *Id.*

The Board of Advisors consists of Joseph Stiglitz and Amartya Sen, two economists who have received the Nobel Memorial Prize in Economic Sciences, and, until his recent death, Sir John Sulston, who was awarded the The Nobel Prize in Physiology or Medicine in 2002. *Id.* ¶6.

iii. KEI is further guided by its constituency via the subscribers to its IP-Health listserv, via regular meetings, and via individual donations from consumers and patients.

The IP-Health listserv mentioned in the Complaint (¶5) with approximately 2400 subscribers consists of patients and consumers, as well as governmental and intergovernmental officials, journalists, advocates and activists and other members of civil society, and the list serves a two-way function — both providing a means for KEI to disseminate information broadly, as well as a means for others outside of KEI to inform KEI's work. Love Declaration, ¶ 58. KEI also regularly convenes meetings and consultations on behalf of and together with its constituency, and is also regularly invited to meet with other groups to discuss the affordability of and access to federally funded medical inventions. *Id.* ¶65.

Furthermore, KEI is transparent with regard to its funding, which includes grants and research contracts from reputable foundations such as the Open Society Foundation and other organizations such as UNITAID, but also includes individual contributions from consumers and patients affected by the high prices of medical technologies. *Id.*, ¶ 59 (“Our ability to obtain funding to advance KEI’s mission depends in large measure on how well we represent patient interests in matters concerning intellectual property rights.”); *See also*

<https://www.keionline.org/about/who-funds-kei>. “If those constituents are dissatisfied with the direction the organization is taking, or with its advocacy efforts, they may then ‘vote with their pocketbooks’ and cease financial support for the organization.” *Citizens Coal Council* at 640. KEI is additionally funded by the Kaiser Foundation Health Plan & Hospitals, a non-profit organization that is also the largest managed care organization in the United States, with 12.2 million members. Love Declaration, ¶59.

KEI has set forth clear facts establishing that Defendants flagrantly violated a variety of statutes and regulations and harmed KEI in ex-ante denying KEI the right of appeal before even permitting KEI to assert why it would merit the appeal, and in admitting to ignoring the black letter obligations of 40 U.S.C. § 559. These acts not only harmed KEI directly but also harmed and were an affront to the interests of consumers and patients and taxpayers in government accountability, and in lower prices for important cancer treatments — especially those funded by taxpayer dollars. KEI has established that it merits associational standing for all of the reasons described above, and this case should proceed.

B. The Functional Equivalency Test Should Not Be Rigidly Applied.

As this case appears to be the first time that the question of the functional equivalency doctrine has arisen in the District of Maryland, and the Court is not bound by the *Heap* decision, it is worth considering that the indicia-of-membership test is not a good fit for many non-member public interest organizations with non-voting constituencies. As Professor Coplan states:

Many public interest environmental organizations are organized as non-membership organizations, or other organizational forms in which the organization's constituency does not vote to select the board of directors or officers of the organization.¹ Typically, these organizations have a "self-perpetuating board of directors, in which the sitting board of directors elects both officers and new board members of the organization."² For these organizations, the question of whether membership voting rights are an essential element of representational standing assumes great importance. A few decisions, with varying results and rationales, have addressed the question of whether voting rights are essential to organizational standing.³

Karl Coplan, *Is Voting Necessary? Organizational Standing and Non-Voting Members of Environmental Advocacy Organizations*, 14 Se. Envtl. L. J. 47, 49 (2005). The article concludes "that voting rights should not be essential to the assertion of representational standing." *Id.*

As Prof. Coplan explains, there are many reasons why nongovernmental organizations would not be structured as traditional membership organizations, as is the case with Plaintiff. These reasons Coplan cites include, for example: added administrative burden; and the potential for "hostile takeover organized by institutions opposed to an organization's advocacy purpose," such as the 2004 proxy battle for control of the Sierra Club (noting that certain "advocacy organizations may be particularly vulnerable given the nature of the issues they take on and the finances available to the institutions they oppose."). *Coplan* at 56-57. Coplan quotes

¹ See Charles H. Steen & Michael B. Hopkins, *Corporate Governance Meets the Constitution: A Case Study of Nonprofit Membership Corporations and Their Associational Standing Under Article III*, 17 Rev. Litig. 209, 211 (1998).

² See Robin Dimieri & Stephen Weiner, *The Public Interest and Governing Boards of Nonprofit Health Care Institutions*, 34 Vand. L. Rev. 1029, 1043 (1981) (discussing nonprofit corporation statutes).

³ See Steen & Hopkins, *supra* note 2, at 221-51.

the ABA Section of Business Law, Nonprofit Governance and Management, 337-54 (V. Futter, ed. 2002):

For most nonprofits serving humanity, the current thinking is to cast as wide a net as possible to further the cause and to communicate electronically with members and nonmembers alike. Supporting a membership, however, is expensive. Cutting-edge nonprofits, particularly mission-driven organizations, will rethink the value of membership to gain the competitive advantage of serving society.

Id.

Thus, rigidly applying the functional equivalency doctrine oversimplifies a complex landscape of public interest organizations and does a disservice to many non-member NGOs that do vital work in the public service, but do not meet the requirements of the test to the t for one reason or another. It is important to note that *Hunt* is not clear as to whether that functional equivalency test was meant to be understood as the minimum requirement. *See* Coplan at p.55 (“[I]n *Hunt* and its progeny, the Supreme Court recognized representational standing for an organization without formal members as long as the traditional indicia of membership were present, but failed to spell out what the irreducible minimum of such indicia were... [and] which of these factors were the bare minimum necessary conditions to representative capacity.”).

There are, as Defendants noted, a variety of cases in various jurisdictions that suggest that the functional equivalency test requires some flexibility in analysis. “These cases illustrate that in this area, the decisions are fact specific, a definitive formal test has yet to be delineated, and most courts have heeded the warning in *Hunt* not to elevate form over substance.” *Citizens Coal Council v. Matt*

Canestrone Contracting, 40 F. Supp.3d 632, 638 (W.D. Pa. 2014) (denying motion to dismiss where associational standing granted and absence of voting rights found not dispositive). These include, for example: “P&A” cases such as *Oregon Advocacy Center v. Mink*, involving Protection and Advocacy Organizations charged with working on behalf of individuals with disabilities, wherein the Court found that mentally disabled constituents had sufficient indicia of membership even though the constituents did not alone choose leadership, and did not alone serve on the board, but where the organization sufficiently identified with and was subject to the influence of those it seeks to represent as to have a “personal stake in the outcome of the controversy.” 322 F.3d 1101 (9th Cir. 2003) (quoting *Baker v. Carr*, 369 U.S. 186, 204, 82 S.Ct. 691 (1962)); See also Kelsey McCowan Heilman, *The Rights of Others: Protection and Advocacy Organizations’ Associational Standing to Sue*, 157 U. Pa. L. Rev. 237 (2008). Other notable cases lend support to a flexible approach, such as *Friends of the Earth v. Chevron Chemical*, 129 F.3d 826 (5th Cir. 1997), where the Court rejected a formulaic approach to the indicia of membership test, and *U.S. Public Interest Research Group v. Bayou Steel*, Civ. A. No. 96–0432, slip op. at 5 (E.D.La. Sept. 15, 1997), wherein USPIRG was granted standing without members and without granting contributors voting rights.

II. Plaintiff has Organizational Standing Because Defendant’s Acts Force KEI to Divert Significant Resources To the Frustration of its Mission

Separate and apart from the fact that Defendants’ claims that Plaintiff lacks associational standing are contradicted by a fair application of the functional

equivalency test and the reasons described *supra*, Plaintiff's organizational standing is established by the substantial diversion of its limited resources toward redressing Defendants' actions, to the detriment of KEI's mission.

The Supreme Court has held that organizational standing may be found where the alleged wrong has caused the organization to "devote significant resources to identify and counteract" the wrong and frustrated the mission of the organization. *Havens Realty Corp. v. Coleman*, 455 U.S. 363, 379, 102 S.Ct. 1114, 71 L.Ed.2d 214 (1982). The Court in that case held that the allegations made by a non-profit organization called Housing Opportunities Made Equal ("HOME") were sufficient to survive a motion to dismiss where the organization alleged that the defendants' racial steering practices caused HOME to divert significant resources and thereby frustrate its mission of assisting equal access to housing through counseling and other referral services. *Id.* "Such concrete and demonstrable injury to the organization's activities—with the consequent drain on the organization's resources—constitutes far more than simply a setback to the organization's abstract social interests." *Id.*

In *Equal Rights Center v. Equity Residential*, this Court similarly held that "an organization suffers an injury-in-fact sufficient to satisfy the first prong of the Article III standing analysis where the organization incurs expenditures in identifying and counteracting [the alleged harm] and those expenditures perceptibly impair the organization's ability to advance its mission." 798 F.Supp.2d 707, 720 (D. Md. 2011). As with the organization in *Havens Realty*, the Equal Rights Center

(“ERC”) was a nonprofit organization dedicated to fair housing practices through education, research, training, counseling, enforcement and advocacy. *Id.* at 712. ERC had alleged that Equity Residential, a housing company, had repeatedly violated the Fair Housing Act; relevant to the organizational standing question, the Court noted that Equity Residential’s acts had caused ERC to divert resources away from its mission, and that the lawsuit itself constituted a diversion of resources. *Id.* at 715.

As with *Havens Realty* and *Equal Rights Center*, KEI has diverted a substantial amount of its resources toward redressing the issues asserted in the Complaint, to the detriment of KEI’s mission as stated in the organization’s Articles of Incorporation:

The Corporation is organized and will be operated exclusively for charitable, educational, and scientific purposes. Specifically, the Corporation will perform research, educate the public and other constituencies, and contribute to policy discourse and debate on issues relating to intellectual property, innovation, economics, international trade, consumer protection, law, and access to knowledge and the fruits of knowledge, including without limitation issues related to the public domain, freely licensed knowledge resources, knowledge resources that are available by custom, access to medical inventions including essential medicines, technologies and business or social systems that are used to manage knowledge resources, modes of stimulating and financing knowledge resources, and related technological, legal and social aspects of the management of knowledge.

Love Declaration, ¶ 2. KEI is a small but effective nonprofit organization, with a staff of seven persons. *Id.*, ¶ 55. One of the seven is counsel, whose primary role is outside of litigation on a variety of time-intensive domestic and international policy and legal and regulatory issues on topics hewing to the issues described in the KEI Articles of Incorporation. *Id.*, ¶56. KEI has spent over 100 hours of time on the

underlying issues and related research and drafting for this litigation, beginning with the original comments submitted to Defendants up through this memorandum, and – but for the personal experiences of outside counsel that resulted in his willingness to accept this case without immediate remuneration – already would have incurred tens of thousands of additional dollars in expenses that would take away from its ability to fulfill its mission. *Id.*, ¶57. That time and eventual expenditure could have been used toward KEI’s mission of meaningfully educating the public and other constituencies, and of contributing to policy discourse and debate, on the issues described in the Articles of Incorporation. *Id.*

For these reasons, KEI should be deemed to have organizational standing.

CONCLUSION

Plaintiff respectfully requests that Defendant’s Motion to Dismiss be DENIED.

_____/s/_____
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Attorneys for Plaintiff

DATED: June 25, 2018

From: Koniges, Ursula (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D5AE2C3139654BC0B9B95718D516310B-KONIGESUM]
Sent: 4/5/2018 3:16:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Dodson, Sara (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=985a956eaa0d4945bdcfd8ea30947d68-dodsonse]
Subject: RE: Opioids – KEI Requests White House Sidestep Naloxone Patents

FYI, Kaleo announced that it's expanding access to its Evzio naloxone injector, and selling it the US gov't agencies at a steep discount ([Reuter's article](#) featured in NIH News Briefing):

Kaleo Expanding Access To Naloxone. Reuters (4/5, Beasley) reports Kaleo Inc. on Thursday "said it is expanding nonprescription access to the Evzio [naloxone] injector and will sell it to U.S. government agencies at a steep discount." Reuters says patients "will need to call a central phone number, talk to a pharmacist, and get Evzio delivered to their door," with Kaleo directly billing insurers. The company last year came under fire "after it raised the price of a twin-pack to \$4,500 from \$690 in 2014."

From: Koniges, Ursula (NIH/OD) [E]
Sent: Wednesday, April 04, 2018 12:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Dodson, Sara (NIH/OD) [E] <sara.dodson@nih.gov>
Subject: RE: Opioids – KEI Requests White House Sidestep Naloxone Patents

NIH Library just shared the Stat+ article (attached) related to the KEI White House request (also attached). Article text below:

White House is urged to sidestep patents on opioid overdose treatment

By ED SILVERMAN / April 2, 2018

The White House is being urged to sidestep patents on a high-priced opioid overdose antidote as one way to stem the rising cost of combating the opioid crisis.

In a [letter](#)¹ sent last Thursday, an advocacy group argues the White House should use a little-known [federal law](#)² that would permit the government to take title to patents on Evzio. This is a decades-old version of naloxone, which is widely used to reverse the effect of opioid and heroin overdoses.

A package of two Evzio auto-injectors at 0.4 mg dosing, which is sold by Kaleo Pharma, has a list — or wholesale — price of \$3,750, according to Truven Health Analytics, an IBM Watson business. The price has jumped from \$575 when the product won regulatory approval in 2014. Meanwhile, a 2 mg dose package has a list price of \$4,100. Several federal agencies, in fact, have recommended increasing access to naloxone, especially for prescription-opioid users, and the high prices have prompted [scrutiny](#)³ from congressional lawmakers. Meanwhile, the

pricing has also strained municipal government budgets because first responders increasingly rely on the product in the wake of the growing number of opioid overdoses around the country.

“A consequence of the high price for the Evzio device is a combination of fiscal strain on the local budgets for first responders, or worse, a lack of access to the technology when it is needed,” Knowledge Ecology International, the advocacy group, wrote to the White House. “The federal government can take action to moderate the price and to expand access to these life-saving technologies.”

So the group is urging the White House to consider using a law that dates back to 1910 and resembles eminent domain: The federal government could use a patented invention without permission, and a drug maker could demand a “reasonable” compensation — such as royalties — but cannot stop the government from taking such a step.

“In this case, the federal government is leading an effort to address the opioid epidemic and searching for ways to save lives. One concrete step would be to notify Kaleo that, unless the company rolls back its 500 percent increased price for Evzio, the U.S. will grant compulsory licenses on all of its patents, and authorize local responders of all types to acquire less expensive versions,” the group wrote.

“By beginning the process of overriding the exclusive rights in the Evzio patents, Kaleo will have a strong incentive to avoid the compulsory license, and the Trump Administration will have an opportunity to lower the prices, and consequently save lives,” KEI argued. “To do nothing is the worst option, since the current outcome is unacceptably bad for first responders and patients.”

This approach has been floated a few times over the past year as government agencies grapple with rising prices for some medicines. Last month, a group of congressional Democrats [urged](#) the Department of Health and Human Services to tap the law in order to sidestep patents on hepatitis C medicines in hopes that lower-cost generics could be manufactured.

As for Kaleo, the company sent us a statement saying it agrees that “the out-of-pocket cost to the patient can be a major barrier to access to naloxone,” and pointed to a scheme in which patients with commercial insurance and a prescription can pay nothing. Those patients who have no government or commercial insurance and have a household income of less than \$100,000, would also pay nothing. For those paying cash, the outlay would be \$360, the company noted last year.

The company has argued that the higher prices are needed to ensure most patients can obtain the product at no cost. Drug makers regularly offer rebates and discounts, so payers frequently pay much less, but Kaleo is counting on enough payers to cover Evzio in order to make a profit, while also underwriting the cost for people who cannot afford its medicine.

The drug maker also maintained that since launching its enhanced patient access program in 2016, more Americans can obtain naloxone for \$0 than ever before. As for the cost to municipal governments. The company replied that “no first responder organization has ever purchased Evzio at the list price. Instead, we have donated more than 300,000 Evzio auto-injectors to hundreds of first responder agencies, public health departments, and qualifying non-profit community groups across 35 states.”

In response KEI’s Jamie Love had this to say: “Kaleo is involved in price gouging, no matter how they spin it. They increased the price by 500 percent overnight to exploit a public health emergency. The fact that they have donations out there is irrelevant, as there are individuals and institutions who cannot access this treatment because of the price. We always hear people complaining about high prices but we don’t see much action. One thing we’ve been trying to focus on at KEI is the fact that in many cases, the government has leverage, and this is one of those cases.”

From: Koniges, Ursula (NIH/OD) [E]

Sent: Tuesday, April 03, 2018 9:37 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Dodson, Sara (NIH/OD) [E] <sara.dodson@nih.gov>

Subject: Opioids – KEI Requests White House Sidestep Naloxone Patents

Latest from KEI via [STAT Plus](#). The letter from KEI to the White House at this [link](#) and attached. I’ll request the article from the NIH Library, and I’ll share it once I receive it.

Group Asks White House To Take Over Patents For Opioid Overdose Reversal Drug.

STAT Plus (4/2, Silverman, Subscription Publication, 32K) reports the advocacy group Knowledge Ecology International wrote a letter (PDF) to the White House urging officials to “sidestep patents” on Evzio’s “decades-old version of naloxone, which is widely used to reverse the effect of opioid and heroin overdoses.” A package of two doses costs \$3,750 – up from \$575 when the medicine won FDA approval in 2014. The group invokes a 1910 law and which says that the federal government “could use a patented invention without permission, and a drug maker could demand a ‘reasonable’ compensation – such as royalties – but cannot stop the government from taking such a step,” according to STAT.

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 6/27/2019 1:41:48 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Burke, Andy (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=305e280edc664e68939d4348603f56e6-burkear]
Subject: RE: Additional inquiry regarding 84 FR 28063, Prospective Grant of an Exclusive Patent License: Development and Commercialization of Cell Therapies for Cancer, to Tailored Therapeutics

Please see below...

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, June 26, 2019 8:02 PM
To: Burke, Andy (NIH/NCI) [E] <andy.burke@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: Re: Additional inquiry regarding 84 FR 28063, Prospective Grant of an Exclusive Patent License: Development and Commercialization of Cell Therapies for Cancer, to Tailored Therapeutics

Richard:

b5

Sent from my iPhone

On Jun 26, 2019, at 2:39 PM, Burke, Andy (NIH/NCI) [E] <andy.burke@nih.gov> wrote:

Hi All,

Additional inquiries from KEI along with my proposed responses. Please let me know if you have any concerns.

Thank you,

Andy

From: Luis Gil Abinader <luis.gil.abinader@keionline.org>
Sent: Wednesday, June 26, 2019 1:58 PM
To: Burke, Andy (NIH/NCI) [E] <andy.burke@nih.gov>
Cc: Jamie Love <james.love@keionline.org>; claire.cassedy <claire.cassedy@keionline.org>
Subject: Additional inquiry regarding 84 FR 28063, Prospective Grant of an Exclusive Patent License: Development and Commercialization of Cell Therapies for Cancer, to Tailored Therapeutics

Dear Andy Burke,

REL0000024123

I am writing in reference to the Federal Register notice 84 FR 28063, Prospective Grant of an Exclusive Patent License: Development and Commercialization of Cell Therapies for Cancer, to Tailored Therapeutics, LLC, for which you are listed as the contact for inquiries. Thank you for your previous response to my colleague Claire Cassidy. We have additional questions about the proposed license.

1. Our research suggests that none of the four patent documents listed in the Federal Register notice has been published online. Have any of them been published?

b5

2. Is <https://tailored-therapeutics.com> the website of the prospective licensee?

b5

3. Is the prospective licensee mentioned in the Federal Register notice 84 FR 28063, Tailored Therapeutics, the same company that appeared as prospective licensee in the Federal Register notice 83 FR 49109, published on September 28, 2018?

b5

4. Was the license proposed in the Federal Register notice 83 FR 49109 executed?

b5

5. Will the exclusive license proposed in the Federal Register notice 84 FR 28063 amend the previous license described in the Federal Register notice 83 FR 49109? In which ways and to what extent?

b5

6. If this is the case, what is the rationale for granting additional exclusive rights to a company that presumably has outstanding obligations under a previous license?

b5

7. Does the license proposed in the Federal Register notice 84 FR 28063 has any relation to the license proposed in the Federal Register notice 84 FR 2537, published on February 7, 2019, which describes Ziopharm Oncology as the prospective licensee? We note that there is a least one patent document, 62/749,750, that is cited in both notices.

b5

Thank you in advance for your assistance,

Luis Gil Abinader

REL0000024123

From: Soukas, Peter (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=B1F6020157AC47948C6E34166B78E433-SOUKASP]
Sent: 6/7/2018 4:38:18 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]
CC: Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]
Subject: RE: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

b5

b5

Thanks.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, June 7, 2018 12:36 PM
To: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <Suzanne.Frisbie@nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <RWILLIAMS@niaid.nih.gov>
Subject: RE: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

b5

From: Soukas, Peter (NIH/NIAID) [E]
Sent: Thursday, June 07, 2018 12:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <Suzanne.Frisbie@nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <RWILLIAMS@niaid.nih.gov>
Subject: FW: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

Dear Mark and Mike,

I just received this email from KEI.

b5

b5

b5

Thanks.

Peter Soukas
National Institutes of Health

REL0000024124

National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: James Love <james.love@keionline.org>

Sent: Thursday, June 7, 2018 12:16 PM

To: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>

Cc: Manon Ress <manon.ress@keionline.org>; luis.gil.abinader@keionline.org; Claire Cassedy
<claire.cassedy@keionline.org>

Subject: Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines

Peter Soukas, Technology Transfer and Patent Specialist,
Technology Transfer and Intellectual Property Office,
National Institute of Allergy and Infectious Diseases,
National Institutes of Health,
Email:

ps193c@nih.gov

Dear Peter Soukas,

We are responding to the request for comments on the Prospective Grant of Exclusive License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Flavivirus Vaccines, to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

*

We note the "

The Licensed Territory may be limited to Europe, China, South Korea, Japan, India, Australia and New Zealand.

"

We oppose granting an exclusive license in the Territory of India, a country with an average income of \$1,670 in 2016, according to the World Bank. India is also a possible source of the vaccine for other developing countries, so the granting of an exclusive license may result in broader restrictions on access.

Sincerely,

James Love
KEI

*

<https://www.federalregister.gov/documents/2018/05/25/2018-11258/prospective-grant-of-exclusive-license-production-of-monovalent-live-attenuated-zika-vaccines-and>

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 8/14/2018 2:08:28 PM
To: Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI Vizamyl Response

Ann— b5

b5

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, August 14, 2018 9:53 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Vizamyl Response

Dale and Mark: Attached are KEI's 5/2018 documents and I just forwarded to you KEI's 8/2018 request that also has attached its 5/2018 documents.

Ann

From: Berkley, Dale (NIH/OD) [E]
Sent: Tuesday, August 14, 2018 9:43 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Vizamyl Response

Ann—could you please send the KEI request that prompts this response?

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, August 14, 2018 9:29 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: KEI Vizamyl Response

REL0000024125

Dear Dale and Mark:

I have attached my draft reply to Ms. Cassidy at KEI requesting a follow-up phone call. Please send me your edits so it can be finalized through Ex. Sec.

Thanks.

Ann

--

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

From: Wertz, Jennifer (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=WERTZJ]
Sent: 6/15/2017 8:48:02 PM
To: Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=jorgensonla]; Fennington, Kelly (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=FENNINGTONKNEW]; Hardesty, Rebecca (NIH/OD) [C] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Hardestyrs2ae]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark
Attachments: CRISPR Patent Policy Response1.doc

Thanks Lyric – the version that Mark emailed yesterday is what was uploaded to DDRMS and is in your queue. I did make minor changes such as putting it on NIH Letterhead, adding the date and removing the email addresses from the body of the letter since Carrie will be emailing it to them once approved. I also added the Acting Chief of Staff to her signature block.

The version of the letter I uploaded is attached.

Jenn

Jennifer L. Wertz
Program Analyst
Office of Science Policy
Office of the Director
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892-7985
Phone: (301) 443-4036
Fax: (301) 496-9839

OSP Website: <http://osp.od.nih.gov>

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OD Voice Website: <http://employees.nih.gov/pages/odvoice/index.aspx>

From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Thursday, June 15, 2017 4:46 PM
To: Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>; Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>; Hardesty, Rebecca (NIH/OD) [C] <rebecca.hardesty@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark

b5 Cc'ing here for confirmation. It is also in Carrie's inbox. It would be good to upload the version they have all weighed in on since it was unclear to me as to whether this would happen once uploaded. Give me a few secs to untangle... will circle back.

REL0000024128

From: Wertz, Jennifer (NIH/OD) [E]
Sent: Thursday, June 15, 2017 4:37 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>; Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>; Hardesty, Rebecca (NIH/OD) [C] <rebecca.hardesty@nih.gov>
Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark

I saw Direct Reply and missed that it said upload draft for director's clearance. Sorry about that. I'll upload the draft into DDRMS right now.

Jenn

Jennifer L. Wertz
Program Analyst
Office of Science Policy
Office of the Director
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892-7985
Phone: (301) 443-4036
Fax: (301) 496-9839

OSP Website: <http://osp.od.nih.gov>
Please follow us on Twitter: @CWolinetzNIH
Subscribe to "[Under the Poliscope](#)" NIH OSP's new blog!

OD Voice Website: <http://employees.nih.gov/pages/odvoice/index.aspx>

From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Thursday, June 15, 2017 4:36 PM
To: Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>; Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>; Hardesty, Rebecca (NIH/OD) [C] <rebecca.hardesty@nih.gov>
Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark

b5

From: Wertz, Jennifer (NIH/OD) [E]
Sent: Thursday, June 15, 2017 4:27 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>; Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>
Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark

Thanks. I sent a draft email and the letter on letterhead to Rebecca to get Carrie's signature (see attached)

Jenn

Jennifer L. Wertz
Program Analyst
Office of Science Policy
Office of the Director
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892-7985
Phone: (301) 443-4036
Fax: (301) 496-9839

OSP Website: <http://osp.od.nih.gov>

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OD Voice Website: <http://employees.nih.gov/pages/odvoice/index.aspx>

From: Jorgenson, Lyric (NIH/OD) [E]

Sent: Thursday, June 15, 2017 4:26 PM

To: Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>; Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>

Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark

I've approved this b5 Will circle back on this tonight.

From: Fennington, Kelly (NIH/OD) [E]

Sent: Thursday, June 15, 2017 3:06 PM

To: Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>; Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>

Subject: RE: reply re CRISP licensing drafted by Ann Hammersla and Mark

Yes, I believe that Lyric has already approved the letter.

Thanks,
Kelly

From: Wertz, Jennifer (NIH/OD) [E]

Sent: Thursday, June 15, 2017 3:04 PM

To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>; Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>

Subject: FW: reply re CRISP licensing drafted by Ann Hammersla and Mark

Is this ok for me to put onto the Word version NIH Letterhead to get Rebecca to have Carrie sign?

Jenn

Jennifer L. Wertz
Program Analyst
Office of Science Policy
Office of the Director
National Institutes of Health
6705 Rockledge Drive, Suite 750

REL0000024128

Bethesda, MD 20892-7985

Phone: (301) 443-4036

Fax: (301) 496-9839

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OD Voice Website: <http://employees.nih.gov/pages/odvoice/index.aspx>

From: Rohrbaugh, Mark (NIH/OD) [E]

Sent: Wednesday, June 14, 2017 3:28 PM

To: Plude, Denise (NIH/OD) [E] <pludedede@mail.nih.gov>; Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>

Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Jorgenson, Lyric (NIH/OD) [E]

<jorgensonla@od.nih.gov>; Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>

Subject: reply re CRISP licensing drafted by Ann Hammersla and Mark

It's direct reply OSP.

Mark L. Rohrbaugh, Ph.D., J.D.

Special Advisor for Technology Transfer

Director, Division of Technology Transfer and Innovation Policy

Office of Science Policy

Office of the Director

National Institutes of Health

b5

b5

From: Myles, Renate (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=RECIPIENTS/CN=MYLESR]
Sent: 2/22/2017 6:37:58 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Wojtowicz, Emma (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wojtowiczeme6d]
Subject: FW: Gizmodo Media Inquiry

Here you go.

b5

From: Myles, Renate (NIH/OD) [E]
Sent: Wednesday, February 22, 2017 1:36 PM
To: 'Kristen Brown' <kristen.brown@gizmodo.com>
Cc: Wojtowicz, Emma (NIH/OD) [E] (emma.wojtowicz@nih.gov) <emma.wojtowicz@nih.gov>
Subject: RE: Gizmodo Media Inquiry

Hi Kristen:

Thanks for checking with us. Please attribute the following response to NIH generally:

NIH has not received a request from KEI about licensing of CRISPR patents.

Here is some background on the statute that guides licensing agreements on inventions supported with federal funding:

The Bayh–Dole Act or University and Small Business Patent Procedures Act, adopted in 1980, is U.S. legislation that sets forth the rights and obligations of the government and federal funding recipients to inventions made from federal government-funded research. Among other things, it gave U.S. universities, businesses, and non-profits the right to assert ownership of their inventions that were made with federal funding. When included in a federal funding agreement, Bayh–Dole permits a grantee or a contractor the right to assert ownership on the inventions it makes with federal funding, but requires the grantee or contractor to make reasonable efforts to commercialize and achieve practical application that the invention is being used and that its benefits are, to the extent permitted by law or government regulations, available to the public on reasonable terms.

Best,
Renate

Renate Myles, MBA
Chief, News Media Branch
National Institutes of Health
Tel: 301-435-3638
Email: mylesr@mail.nih.gov
Web: <http://www.nih.gov>

NIH . . . Turning Discovery Into Health

Celebration of Science at NIH: *watch how medical research saves lives and improves health*

From: Kristen Brown [<mailto:kristen.brown@gizmodo.com>]
Sent: Wednesday, February 22, 2017 11:31 AM
To: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>
Subject: Re: Gizmodo Media Inquiry

Yep! Story running in a few hours

Sent via iMagic.

REL0000024129

On Feb 22, 2017, at 6:21 AM, Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov> wrote:

Hi Kristen:

My apologies; I missed your email from yesterday. Are you still looking for a response?

Thanks,
Renate

Renate Myles, MBA
Chief, News Media Branch
National Institutes of Health
Tel: 301-435-3638
Email: mylesr@mail.nih.gov
Web: <http://www.nih.gov>

NIH . . . Turning Discovery Into Health

Celebration of Science at NIH; watch how medical research saves lives and improves health

From: Kristen V. Brown [<mailto:kristen.brown@gizmodo.com>]
Sent: Tuesday, February 21, 2017 9:41 AM
To: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>
Subject: Gizmodo Media Inquiry

Hi Renate,

I'm planning a piece for Wednesday when Knowledge Ecology International files to ask the federal government to develop a policy to "ensure that the licensing of [the CRISPR] patents is as open and non-discriminatory as possible." (A little more info on this, [via STAT](#).) They plan to do so under laws that would allow the NIH, as a funder of the CRISPR work, to step in if licensing is not happening under reasonable terms. However I know that there is no case in which the federal government has actually exercised that right.

Can the NIH comment on how it will review and respond to this filing? My deadline is EOD today.

Thanks!

Kristen V. Brown
senior writer, gizmodo

b6

REL0000024129

From: Reczek, Peter (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=RECZEKPRD1E]
Sent: 5/21/2015 2:39:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: New patent law suits down
Attachments: Gleevec Case Study_pr.docx

Mark

Interesting.

b5

I'm attaching my notes on the VOBR search re: Gleevec. Could you please have a look and see what you think.

b5

but any comments would be most welcome.

Cheers,
Peter

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, May 21, 2015 10:32 AM
To: Reczek, Peter (NIH/OD) [E]; Jorgenson, Lyric (NIH/OD) [E]; Volkov, Marina (NIH/OD) [E]; Wolinetz, Carrie (NIH/OD) [E]; Carr, Sarah (NIH/OD) [E]; Berkson, Laura (NIH/OD) [E]; Culhane, Ned (NIH/OD) [E]
Subject: FW: New patent law suits down

http://www.washingtonpost.com/blogs/the-switch/wp/2015/05/21/new-patent-lawsuits-are-down-for-the-first-time-in-five-years-heres-why-thats-a-huge-deal/?tid=hpModule_88854bf0-8691-11e2-9d71-f0feafdd1394&hpid=z14

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Office of Intramural Research
National Institutes of Health

REL0000024130

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b5

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 6/26/2018 4:03:55 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
Subject: RE: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion

No not really. There's a hearing scheduled for October 15 but the judge could rule on the motions before that.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 26, 2018 12:02 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>; Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: RE: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion

Any idea when the judge will rule on it?

From: Berkley, Dale (NIH/OD) [E]
Sent: Tuesday, June 26, 2018 11:58 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Activity in Case 8:18-cv-01130-PJM Knowledge Ecology International v. National Institutes of Health et al Response in Opposition to Motion

Attached is KEI's response to our motion to dismiss, just for your information, no action necessary. Please distribute to any others in management who have an interest or need to know. b5

b5

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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REL0000024131

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 1/2/2019 5:10:35 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: question

Ok thanks, b5

b5

b5 Could you do that?

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, January 02, 2019 12:02 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: question

In case this is useful:

b5

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, January 02, 2019 10:27 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: question

Mark— b5

b5

Many thanks, Dale

From: Lazerow, Alan (USAMD) <Alan.Lazerow@usdoj.gov>
Sent: Wednesday, January 02, 2019 9:54 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: question

b5

Alan C. Lazerow | Assistant United States Attorney
United States Attorney's Office, District of Maryland
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REL0000024132

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, January 2, 2019 9:46 AM
To: Lazerow, Alan (USAMD) <ALazerow@usa.doj.gov>
Subject: RE: question

Alan:

b5

Thanks, Dale

From: Lazerow, Alan (USAMD) <Alan.Lazerow@usdoj.gov>
Sent: Sunday, December 30, 2018 10:24 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: question

Dale – b5

b5

Alan

Alan C. Lazerow | Assistant United States Attorney
United States Attorney's Office, District of Maryland
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REL0000024132

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 8/14/2018 1:53:09 PM
To: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI Vizamyl Response
Attachments: KEI Summary Vizamyl - 05-22-2018 pm.docx; KEI-Briefing-Note-2018-1.pdf; Azar-KEI-CoverLetter-Vizamyl-patents-18May2018.pdf

Dale and Mark: Attached are KEI's 5/2018 documents and I just forwarded to you KEI's 8/2018 request that also has attached its 5/2018 documents.

Ann

From: Berkley, Dale (NIH/OD) [E]
Sent: Tuesday, August 14, 2018 9:43 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Vizamyl Response

Ann—could you please send the KEI request that prompts this response?

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, August 14, 2018 9:29 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: KEI Vizamyl Response

Dear Dale and Mark:

I have attached my draft reply to Ms. Cassidy at KEI requesting a follow-up phone call. Please send me your edits so it can be finalized through Ex. Sec.

Thanks.

Ann

--

Ann M. Hammersla, J.D.
Director

REL0000024136

Division of Extramural Inventions and Technology Resources
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**KNOWLEDGE ECOLOGY INTERNATIONAL'S
REQUEST DATED May 18, 2018
FOR NIH TO TAKE OWNERSHIP OF
VIZAMYL (INN FLUTEMETAMOL F 18) PATENTS**

Summary of KEI Request:

KEI identified in the FDA Orange Book, four patents for **VIZAMYL** (INN flutemetamol F 18) an imaging drug used to evaluate possible cases of Alzheimer's disease or other causes of cognitive decline in the as patents. KEI indicates that Vizamyl is available in 10 or 30 mL multi-dose glass vials at a strength of 150 MBq/mL (4.05 mCi/mL), the price of 1 vial (5 mCi) is approximately \$28,000. Medicare restricts reimbursements for the tests.

The four **VIZAMYL patents** are assigned to the **University of Pittsburgh by three University of Pittsburgh Inventors** (Attachment 1) and according to USPTO records licensed to GE Healthcare.

KEI asks the Secretary's office and the National Institutes of Health (NIH) to investigate a failure by the University of Pittsburgh to disclose NIH research funding on the four VIZAMYL patents.¹ None of the VIZAMYL patents indicate government support. Based on this alleged failure to disclose, KEI asks the NIH to take title to the patents. At a minimum, KEI is requesting that the Department of Health and Human Services require the University of Pittsburgh to correct the failure to disclose the NIH grants in these patents.

Contrary to KEI's assertion, DEITR has found that the Subject Inventions leading to the four VIZAMYL patents were disclosed to the NIH and DOE. However, these records were subsequently voided, cutting off further reporting obligations, based on the University of Pittsburgh's assertion that there was no government funding.

Recommendations:

Review NIH grants and publications with NIH Program Officials to correlate the specific aims and progress reports to the specification of identified patent applications and issued patents.

If correlation is found, in recent similar cases, the NIH has required compliance with the Bayh-Dole Act (a term and condition of NIH awards). When previously required, other non-profits and for-profit corporations resolved all non-compliance issues within the timeframe provided.

At a minimum, NIH should reverse its previous decision to void the reported Inventions and require the University of Pittsburgh to complete all reporting requirements for the four VIZAMYL patents within ten days of NIH notice of non-compliance.

For all other NIH supported grants, require the University of Pittsburgh to complete all Bayh-Dole Act compliance requirements within 120 days of NIH's notice of non-compliance.

¹ An additional U.S. Patent, 8,916,131 is listed in the FDA Orange Book for VIZAMYL that was assigned to GE Healthcare, Ltd. and KEI has not requested any further NIH investigation into potential government rights regarding this patent

Depending on further factual development, discussion with OPERA, OER, OSP (Mark Rohrbaugh) and OGC (Dale Berkley) on the NIH's compliance efforts and other steps to consider in this case.

Details of KEI's Request and NIH Findings to date:

- KEI's request asserts that the same three named inventors, on each of the four VIZAMYL patents, Klunk, Mathis, and Wang received more than \$66 million in federal funding. Using the NIH RePORTER, KEI identified NIH multiple awards to the University of Pittsburgh.
- From 1988 to 2018, William Klunk was indicated as a PI on multiple projects or sub-projects totaling \$47,209,483. From 1986 to 2018, with Chester A. Mathis, Jr. as an investigator totaling \$14,936,292. From 2003 to 2013, with Yanming Wang was an investigator totaling \$4,116,038.
- KEI Identified a total of 11 possible awards to the University of Pittsburgh, over multiple budget periods, involving the three named Inventors that are possibly related to the VIZAMYL patents including (3) related to U.S. **7,270,800** and U.S. **7,351,401**. KEI highlighted one award (MH053310) due to end of the project period being two months before the Priority Date of the patents.
- KEI indicates that these NIH Grants are directly related to the four VIZAMYL patents and that this funding from the NIH and the U.S. Department of Energy, (DOE) was acknowledged in related academic papers. KEI's request includes references to four specific publications (Attachment 2).
- DEITR has located records in iEdison and its repository indicating that the University of Pittsburgh had reported to the NIH and DOE **four separate Subject Inventions** between **June 26, 2000** and **January 10, 2005** and **five patent applications** related to the four VIZAMYL patents including the initial provisional application that two of the VIZAMYL patents claim priority to.
- DEITR also located conflicting correspondence from the University of Pittsburgh dated **June 10, 2002** indicating that one award (MH 053310) should not have been included in the Invention Report. This correspondence also included an acknowledgement by Inventor Klunk that three other awards were involved and that he'd "rather proceed carefully and ***consider the current federal support as being crucial to the current embodiment of the invention.***"
- DEITR also found later correspondence from University of Pittsburgh dated **June 27, 2007** requesting that the NIH void these Invention Reports and Patents in the iEdison system based on a statement from the PI, William Klunk that there was no government funding involved in the Inventions.
- DEITR is unable to verify from its records whether the 2002 correspondence was reviewed and considered when the records were voided in 2007.
- KEI's request outlines the statutory and regulatory basis for NIH to take title to the NIH-funded patents. 37 CFR 401.14 (c) and (d).

May 22, DEITR

Attachment 1

Four patents in the FDA Orange Book for VIZAMYL (INN FLUTEMETAMOL F 18)

1. U.S. **7,270,800** filed March 14, 2003 and issued September 1, 2007.
 - a. Patent Title: **Thioflavin derivatives for use in antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition**
 - b. Priority Date: August 24, 2000²
 - c. Assignees: University of Pittsburgh³, GE HEALTHCARE LIMITED⁴ (License)
 - d. Inventors: William E. Klunk, Chester A. Mathis JR., Yanming Wang
 - e. PCT Application Filing Date: March 15, 2004
 - f. Patent Expiration Date: September 03, 2025
2. U.S. **7,351,401** filed June 3, 2004 and issued April 1, 2008
 - a. Patent Title: **Thioflavin derivatives for use in the antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition**
 - b. Priority Date: August 24, 2000
 - c. Assignees: University of Pittsburgh⁵
 - d. Inventors: William E. Klunk, Chester A. Mathis JR., Yanming Wang
 - e. Patent Expiration Date: January 24, 2023
3. U.S. **8,236,282** filed September 30, 2009 and issued August 7, 2012.
 - a. Patent Title: **Benzothiazole derivative compounds, compositions and uses**
 - b. Priority Date: August 22, 2003: Continuation Application of U.S. Ser. No. 10/645,847
 - c. Assignees: University of Pittsburgh (name change assignment).
 - d. Inventors: William E. Klunk, Chester A. Mathis JR., Yanming Wang
 - e. Patent Expiration Date: May 21, 2024.
4. U.S. **8,691,185** filed July 12, 2012 and issued April 8, 2014.
 - a. Patent Title: **Benzothiazole derivative compounds, compositions and uses**
 - b. Priority Date: August 22, 2003, Continuation Application of U.S. Ser. No. 12/570,379, filed Sep. 30, 2009, now U.S. Pat. No. 8,236,282, which is a Continuation Application of U.S. Ser. No. 10/645,847 filed Aug. 22, 2003 now abandoned.
 - c. Assignees: No assignments recorded at USPTO
 - d. Inventors: William E. Klunk, Chester A. Mathis JR., Yanming Wang
 - e. Patent Expiration Date: January 24, 2023

² Priority is claimed from U.S. Provisional Application 60/227,601 filed August 24, 2000 and related U.S. Non-Provisional Application, 09/935,767 filed August 24, 2001.

³ Assignment dated February 1, 2008 by Inventor Mathis, February 20, 2008 by Inventor Klunk, and March 24, 2008 by Inventor Wang.

⁴ Exclusive License from the University of Pittsburgh to GE Healthcare Limited executed by the University of Pennsylvania on June 23, 2005 in foreign and domestic patent applications including U.S. Non-Provisional Application, 09/935,767 filed August 24, 2001.

⁵ Assignment dated February 1, 2008 by Inventor Mathis, February 20, 2008 by Inventor Klunk, and March 24, 2008 by Inventor Wang.

Attachment 2

KEI Publication references related to the VIZAMYL Patents

(2008). Klunk WE; Mathis CA. " Whatever happened to Pittsburgh Compound-A? " Alzheimer Dis Assoc Disord. 22(3):198-203.

(2003). Bacskai BJ; Hickey GA; Skoch J; Kajdasz ST; Wang Y; Huang GF; Mathis CA; Klunk WE; Hyman BT. " Four-dimensional multiphoton imaging of brain entry, amyloid binding, and clearance of an amyloid-beta ligand in transgenic mice. " Proc Natl Acad Sci U S A. 100(21):12462-7

(2004). Klunk WE; Engler H; Nordberg A; Wang Y; Blomqvist G; Holt DP; Bergström M; Savitcheva I; Huang GF; Estrada S; Ausén B; Debnath ML; Barletta J; Price JC; Sandell J; Lopresti BJ; Wall A; Koivisto P; Antoni G; Mathis CA; Långström B. " Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. " Ann Neurol. 55(3):306-19.

(2004). Wang Y; Klunk WE; Debnath ML; Huang GF; Holt DP; Shao L; Mathis CA. " Development of a PET/SPECT agent for amyloid imaging in Alzheimer's disease. " J Mol Neurosci. 24(1):55-62.

Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions

KEI Briefing Note: 2018:1. Andrew Goldman. Revised March 16, 2018

Legal, Regulatory, and Contractual Obligations¹

The Bayh-Dole Act and federal regulations and guidelines make clear several obligations for contractors in the disclosure of government rights in subject inventions, including: (1) a requirement to disclose that federal funding contributed to an invention; (2) contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

First, contractors are required to disclose subject inventions discovered with federal funding in a timely manner and with sufficient detail to describe the invention.

Under 35 U.S.C. § 202(c)(1), any contractor that receives funding from the federal government is required to “disclose each subject invention to the Federal agency within a reasonable time after it becomes known to contractor personnel responsible for the administration of patent matters.”²

Under 37 C.F.R. § 401.3(a), each federal funding agreement shall contain the “standard patent rights clause” found at 37 C.F.R. § 401.14(a), barring specific circumstances and exceptions.³ Subsection (c)(1) of the patent rights clause outlines the disclosure requirements, including a two month time limit on the disclosure of patents and a requirement that the disclosure have sufficient detail:⁴

37 C.F.R. § 401.14(a)(c)(1)

(c) Invention Disclosure, Election of Title and Filing of Patent Application by *Contractor*

(1) The *contractor* will disclose each subject invention to the *Federal Agency* within two months after the inventor discloses it in writing to *contractor* personnel responsible for patent matters. The disclosure to the *agency* shall be in the form of a written report and shall identify the contract under which the invention was made and the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or

¹ See: <https://www.keionline.org/bayh-dole/failure-to-disclose>

² The statute defines a “subject invention” at 35 U.S.C. § 201(e) as “any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement,” and defines a contractor at 35 U.S.C. § 201(c) as “any person, small business firm, or nonprofit organization that is party to a funding agreement.”

³ The exceptions do not contain reference to the disclosure requirements.

⁴ Italics in original.

electrical characteristics of the invention. The disclosure shall also identify any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure. In addition, after disclosure to the *agency*, the *Contractor* will promptly notify the *agency* of the acceptance of any manuscript describing the invention for publication or of any on sale or public use planned by the *contractor*.

...

(4) Requests for extension of the time for disclosure, election, and filing under subparagraphs (1), (2), and (3) may, at the discretion of the *agency*, be granted.

Second, in implementing this regulation, agencies may require disclosure through documentation and/or via iEdison, an online electronic system for reporting inventions and patents discovered under federal grants, or via other documents to be submitted.⁵ iEdison is run by the National Institutes of Health (NIH), but is used by a wide variety of agencies, including:

Agency for Health Care Research and Quality (AHRQ)
Agricultural Research Service (ARS)
Agency for Toxic Substances and Disease Registry (ATSDR)
Air Force Office of Scientific Research (AFOSR)
Air Force Research Laboratory Information Directorate (AFRL/RI)
Air Force Materiel Command Legal Office (AFMCLO/JAZ)
Army Medical Research and Materiel Command (ARMY/MRMC)
Army Natick Soldier Systems Center (ARMY/SSC)
Army Research Laboratory (ARMY/ARL)
Army Research Office (ARMY/ARO)
Army Space and Missile Defense Command (ARMY/SMDC)
Centers for Disease Control and Prevention (CDC)
Defense Advanced Research Projects Agency (DARPA)
Defense Microelectronics Activity (DMEA)
Defense Threat Reduction Agency (DTRA)
Department of Energy (DOE)
Department of Homeland Security
Science and Technology Directorate (DHS/S&T)
Department of Transportation (DOT)
Economic Development Administration (EDA)
Environmental Protection Agency (EPA)
Food and Drug Administration (FDA)
Indian Health Service (IHS)

⁵ iEdison.gov

International Trade Administration (ITA)
National Institute of Food and Agriculture (NIFA)
National Institutes of Health (NIH)
National Institute of Standards and Technology (NIST)
National Oceanic and Atmospheric Administration (NOAA)
National Science Foundation (NSF)
Nuclear Regulatory Commission (NRC)
Office of Naval Research (ONR)
U.S. Agency for International Development (USAID)
United States Forest Service (USFS)

iEdison was created in 1995 in the wake of findings by the Office of Inspector General of the Department of Health and Human Services that the NIH was not sufficiently overseeing and monitoring compliance with Bayh-Dole requirements, including disclosure.⁶

By way of example of how agencies require disclosure, the NIH requires contractors to disclose subject inventions via iEdison, as well as via HHS Form 568, entitled, "Final Invention Statement and Certification (For Grant or Award)," available at: <https://grants.nih.gov/grants/hhs568.pdf>.

The NIH specifies the required information on a FAQ related to the use of iEdison, and also notes that contractors should disclose the subject invention even if they have, in the past, failed to report the invention within the two month period:⁷

5. What information is required to report a subject invention?

The invention disclosure must include the following information:

- Either the EIR Number, Invention Docket Number, or both.
- Invention Title
- Names of all of the inventors and the institutions with which they are associated
- Invention Report Date
- Description of the Invention that must meet the standards set forth per 37 CFR Sec. 401.14 (a)(c)(1):

"... be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of

⁶ <https://oig.hhs.gov/oei/reports/oei-03-91-00930.pdf>

⁷ Available at: https://era.nih.gov/iedison/iedison_faqs.cfm#VIII5 (accessed Jan. 6, 2017).

the invention.”37 C.F.R. 401.14(a)(c)(1)”

-Primary Funding Agency

-All funding agreement numbers and names of the funding agencies

- Any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure

9. If I upload a patent application, can that patent application satisfy the Invention Disclosure Report requirement?

Yes, so long as the EIR Number or Invention Docket Number is included on the submission, the patent record containing the patent/patent application number has been reported in iEdison, and you upload proof that the patent application was filed with the USPTO, e.g., a USPTO submission receipt.

10. What should a grantee/contractor do if a subject invention hasn't been reported to the awarding agency within the required 2 month period?

Always report the invention, even if it is late. The invention report date should be the date the inventor notified the awardee institution of the subject invention. Provide an explanation in the "Explanatory Notes" section of the invention record.

On February 17, 2016, NIH issued a notice entitled “Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison.” The notice explained that failure to disclose the subject invention via both iEdison and Form 568 could result in the loss of rights in the invention.⁸

Finally, under 35 U.S.C. § 202(c)(6) and 37 C.F.R. § 1.77(b)(3), contractors are required to state within the patent application that the federal government contributed funding to support the discovery of the invention and that the government retains certain rights:

35 U.S.C. § 202(c)(6)

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

⁸ National Institutes of Health, Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison, NOT-OD-16-066 (Feb. 17, 2016), NIH Guide Notice, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-066.html>.

(6) An obligation on the part of the contractor, in the event a United States patent application is filed by or on its behalf or by any assignee of the contractor, to include within the specification of such application and any patent issuing thereon, a statement specifying that the invention was made with Government support and that the Government has certain rights in the invention.

35 C.F.R. § 1.77(b)(3)

(b) The specification should include the following sections in order:

...

(3) Statement regarding federally sponsored research or development.

The Manual of Patent Examining Procedure contains the following recommended language:

“This invention was made with government support under (identify the contract) awarded by (identify the Federal agency). The government has certain rights in the invention.”⁹

Remedies for Non-Disclosure

Non-disclosure Permits the Federal Government to Receive Title to the Invention

Failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the Federal Government to “**receive title to any subject invention not disclosed to it within such time**” (emphasis added).

The patent rights clause at 37 C.F.R. § 401.14(a) specifies this right to claim title in subsection (d):

37 C.F.R. § 401.14(a)

(d) Conditions when the Government May Obtain Title

The contractor will convey to the Federal agency, upon written request, title to any subject invention—

(1) If the contractor fails to disclose or elect title to the subject invention within the times specified in (c), above, or elects not to retain title; provided that the agency may only request title within 60 days after learning of the failure of the contractor to disclose or elect within the specified times.

⁹ MPEP (9th ed. Rev. 07.2015, Nov. 2015), § 310.

...

In the past, the Federal Government has utilized its authority to claim title in subject inventions that have not been properly disclosed, as in the case of *Campbell Plastics Engineering & Mfg., Inc. v. Brownlee*, 389 F.3d 1243 (Fed. Cir. 2004) (finding that federal government claim of title in invention was legitimate under federal acquisition regulations and supported by the Bayh Dole Act where disclosure submissions were “piecemeal” and violated the contractual agreement with the government); see also *Central Admixture Pharmacy Services, Inc. v. Advanced Cardiac Solutions, P.C.*, 482 F.3d 1347, 1352-53 (Fed. Cir. 2007) (“Critically, *Campbell Plastics* holds that a Bayh–Dole violation grants the government *discretionary* authority to take title. . . . When a violation occurs, the government can choose to take action; thus, title to the patent may be voidable.”).

In *Campbell Plastics*, the court found that the contract was clear and unambiguous, but moreover the government’s claim to title was “buttressed by the policy considerations behind the Bayh Dole Act.” *Id.* at 1248. These include, specifically under 35 U.S.C. § 200, the need “to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions.”

Correction of the Patent Will Establish Other Enforceable Rights For the Federal Government

Even if the Government permits the continued use of its invention, forcing a correction to the patent will create enforceable obligations and rights designed to protect the public interest. These rights can be used as leverage to force concessions in pricing.

Local Manufacturing

Under 35 U.S.C. § 204, for example, there is a requirement (waivable in individual cases) that the subject invention be manufactured substantially in the United States.¹⁰

35 U.S.C. § 204

Notwithstanding any other provision of this chapter, no small business firm or nonprofit organization which receives title to any subject invention and no assignee of any such small business firm or nonprofit organization shall grant to any person the exclusive right to use or sell any subject invention in the United States unless such person agrees that any products embodying the subject invention or produced through the use of the subject invention will be manufactured substantially in the United States. However, in individual cases, the requirement for such an agreement may be waived by the Federal agency under whose

¹⁰ See also the patents rights clause regarding preference for United States industry at 37 C.F.R. § 401.14(a)(i).

funding agreement the invention was made upon a showing by the small business firm, nonprofit organization, or assignee that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible.

Practical Application

Government rights in a subject invention also implicates the requirement repeated in numerous sections of the Bayh-Dole Act that there be “practical application” of the invention, including once in 35 U.S.C. § 203 on march-in rights, and nine times in 35 U.S.C. § 209 on licensing federally-owned inventions. “Practical application” is defined under 35 U.S.C. § 201(f) to mean “manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized **and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.**” (Emphasis added.)

The phrase “available to the public on reasonable terms” to is a statutory obligation in the Bayh-Dole Act that only has meaning if the invention is available at a reasonable price, and while the NIH has been loath to enforce this requirement, the Congress is increasingly focused on a practical implementation of such an obligation. For example, in 2017, the Senate Armed Services Committee adopted a directive in a committee report to require enforcement of this obligation when the prices of a medical technology were higher in the United States than the median price charged in seven countries with large economies with at least 50 percent of U.S. per capita income.¹¹ There is also U.S. and international case law, as well as statutes in the U.K. and South Africa, defining the phrase “reasonable terms” to include the price of a product of service.¹²

March-In Rights and the Royalty-Free Right

Under 35 U.S.C. § 203(a), the government may require the grant of a license to a third party, or may grant such a license itself, if any of four conditions are met, including the obligation of practical application:

35 U.S.C. § 203

¹¹ 115TH Congress, 1st Session, 2017, Senate Report 115–125. National Defense Authorization Act for Fiscal Year 2018. Report to accompany S. 1519, page 173.

¹² See KEI 10 March 2017 Comments on Army Exclusive License on Zika Virus Vaccine Patents to Sanofi, available at https://www.keionline.org/wp-content/uploads/2017/03/KEI-March_10_2017-3rd-Comments-Zika.pdf.

(a) With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such—

- (1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
- (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
- (3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
- (4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.

The government also retains a perpetual non-exclusive royalty-free license in the invention, written into any funding agreement under 35 U.S.C. § 202(c)(4), and again iterated as a required term and condition for any license of a federally-owned invention under § 209(d)(1). The royalty-free right, as opposed to the march-in rights, has no precondition and can be used at any time, for any reason.

35 U.S.C. § 202

...

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

(4)

With respect to any invention in which the contractor elects rights, the Federal agency shall have a nonexclusive, nontransferrable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world: Provided, That the funding agreement may provide for such additional rights, including the right to assign or have assigned foreign patent rights in the subject invention, as are determined by the agency as necessary for meeting the obligations of the United States under any treaty, international agreement, arrangement of cooperation, memorandum of understanding, or similar arrangement, including military agreement relating to weapons development and production.

35 U.S.C. § 209

...

(d) Terms and Conditions.—Any licenses granted under section 207(a)(2) shall contain such terms and conditions as the granting agency considers appropriate, and shall include provisions—

(1)

retaining a nontransferable, irrevocable, paid-up license for any Federal agency to practice the invention or have the invention practiced throughout the world by or on behalf of the Government of the United States;

...

Both of these rights provide significant leverage to the United States, as they could be used to allow affordable competition. Even the viable threat of use of either of these rights might be sufficient to prompt price reductions or other concessions increasing access while decreasing price.

In some cases there may be more than one patent in a particular medicine, and not all patents may have government rights. In the event that there is at least one patent with government rights, the government could potentially use the royalty-free right in conjunction with the government use provision of 28 U.S.C. § 1498. While § 1498 has been used many times by the military, interest in using the government use law alone on medical technologies has been complicated by uncertainty as to the extent of compensation owed.¹³ Using the royalty-free right and § 1498 together would lessen the amount of compensation owed to the patent holder.

¹³ See, e.g. May 12, 2015 letter from Senator Bernard Sanders to Secretary of the US Department of Veterans Affairs, Robert McDonald.
<https://www.keionline.org/wp-content/uploads/2015/05/12may2015-Sanders-McDonald-Veterans-1498.pdf>; and <https://www.keionline.org/22842>.



May 18, 2018

The Honorable Alex Azar
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Via email: secretary@hhs.gov

Re: Investigation into the failure disclose NIH funding in inventions patented by the University of Pittsburgh for flutemetamol F 18),

Dear Secretary Azar:

We are writing to ask the Department of Health and Human Services (HHS) to investigate and if applicable, to remedy a failure to disclose National Institutes of Health (NIH) funding in four inventions patented by the University of Pittsburgh. The four inventions are identified in the FDA Orange Book as patents for Vizamyl (INN flutemetamol F 18), used to evaluate possible cases of Alzheimer's disease or other causes of cognitive decline. Access to the tests is currently restricted, including restrictions on reimbursements by Medicare.

Knowledge Ecology International (KEI) asks that HHS take title to the four patents. The legal basis for the proposed remedy is set out in the attached memorandum, *Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions*.¹ One of the possible remedies for non-disclosures, as set out in 35 U.S.C. § 202(c)(1) and 37 C.F.R. § 401.14, is for the federal government to take possession of the patent title.

We believe this is an egregious case of non-disclosure. The same three inventors are listed for each of the four patents. Collectively they were the principal investigators in NIH grants involving more than \$66 million.

- According to the NIH RePORTER database, from 1988 to 2018, William Klunk was the principal investigator for grants obtained from the NIH consisting of 52 projects, 35 sub-projects and a total funding amount of \$47,209,483.

¹ Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions. KEI Briefing Note: 2018:1. Andrew Goldman. Revised March 16, 2018.

- From 1986 to 2018, Chester A. Mathis, Jr. received NIH grants consisting of 31 projects and 12 subprojects with a total funding amount of \$14,936,292.
- From 2003 to 2013, Yanming Wang was listed as the principal investigator for 19 NIH projects involving \$4,116,038 of funding.

This actually understates the amount of federal funding involved, since the inventors have also received NIH research contracts and funding from the Department of Energy for this research.

The inventors have made references to NIH and DOE funding of their work in papers describing the inventions, but did not report the grants on the patents, and the patents do not appear in the NIH RePORTER database.

The patents were subsequently licensed to GE Healthcare. We believe the public interest would be served if the patents were licensed on a non-exclusive basis, permitting more competition in the use of the inventions, resulting in greater innovation and lower prices. Lower prices for flutemetamol F 18 may expand access to the test, which, as Medicare describes, “may be clinically useful in the work up and management of patients with cognitive impairment who are being evaluated for possible Alzheimer’s disease or other causes of cognitive decline.”²

Finally, we note that this one of several letters we have sent to the HHS and/or the NIH, regarding failure of NIH grant recipients to disclose federal funding. We are still waiting to hear the conclusions of investigations regarding Cold Spring Harbor patents on nusinersen (trade name Spinraza), the Pharmasset/Gilead patent on sofosbuvir, the Dana Farber Cancer Institute patents on midostaurin (Trade name Rydapt), multiple institutions’ (including an NIH-funded project at a foreign university) patents on Exondys 51, and the University of Pennsylvania patents on Lomitapide (trade name Juxtapid). We are making these inquiries as a public service, to ensure the public has the opportunity to benefit from the safeguards and public interest provisions in the Bayh-Dole Act, including the obligation by patent holders to make the inventions available to the public on reasonable terms, the ability of the NIH to ensure broad use of inventions for research purposes, and the requirements in the Bayh-Dole Act for domestic manufacturing of products, among other requirements.

Sincerely,



James Love, Director, KEI
james.love@keionline.org
+1.202.332.2670

² <https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/Amyloid-PET.html>

Attachments

1. Vizamyl (INN flutemetamol F 18): Failures to disclose NIH funding for four patents in the FDA Orange Book invented by William Klunk, Chester Mathis, Jr., and Yanming Wang, and assigned to the University of Pittsburgh. Knowledge Ecology International, May 18, 2018.
2. KEI-Briefing-Note-2018-1

Cc:

Dr. Francis Collins, Director, the National Institutes of Health: Francis.Collins@nih.hhs.gov

The Honorable Daniel R. Levinson, Inspector General, Office of Inspector General (OIG), HHS, Dan.Levinson@oig.hhs.gov

Ann M. Hammersla, J.D., Director, Division of Extramural Inventions and Technology Resources Office of Policy for Extramural Research Administration, hammerslaa@od.nih.gov

Rep. Tom Cole, Oklahoma, Chairman, Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, House of Representatives.

Rep. Rosa DeLauro, Connecticut, Ranking Member, Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, House of Representatives.

Roy Blunt, Chair, Labor, Health and Human Services, Education and Related Agencies, Committee on Appropriations, U.S. Senate

Patty Murray, Ranking Member, Labor, Health and Human Services, Education and Related Agencies, Committee on Appropriations, U.S. Senate

From: Joe Allen [jallen@allen-assoc.com]
Sent: 10/5/2016 11:58:13 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: House Dems urge Pres Obama to use to Bayh-Dole to control drug prices

This is from today's Huffington Post. There's also a video of the press conference when they released the letter which I couldn't copy:

THE BLOG

The President Can Act Against Drug Company Rip-Offs. These House Dems Explain.

10/05/2016 03:05 pm ET

Rep. Mark Pocan speaks with Richard Eskow on The Zero Hour

This week I spoke with Rep. Mark Pocan (D, WI) about an open letter to President Obama he is circulating to fellow members of Congress this week. It's an important letter, not only for its subject matter - it addresses our current crisis in runaway drug costs - but because it explains how the White House can address this issue without the need to pass legislation in the Republican-controlled House.

Most of us already know we've got a problem. A Kaiser survey released last week shows that 77 percent of Americans believe that "prescription drug costs are unreasonable."

They're right. As the letter notes, Gilead Sciences recently set a price of \$84,000 for its 12-week course of Hepatitis C treatment - even though, as activist Annette Gaudino explained last August on The Zero Hour, it charges a fraction of that cost in other countries and still turns a profit. The letter also attacks the "price-gouging and anti-competitive behavior" of Mylan Pharmaceuticals, which jacked up the price of an EpiPen by nearly 500 percent over a five-year period.

Rep. Pocan's letter urges President Obama to "use executive action and take concrete steps" to address the drug cost crisis, and lists three tools that the president can use. The first is the Bayh-Dole Act, which gives the National Institutes of Health the power to ensure that medications that were developed at taxpayer expense are accessible to the public at affordable rates.

Next, the president can use the authority granted to the Secretary of Health and Human Services, under the Medicare Drug Act of 2003, to allow the importation of lower-cost drugs from other countries under certain conditions.

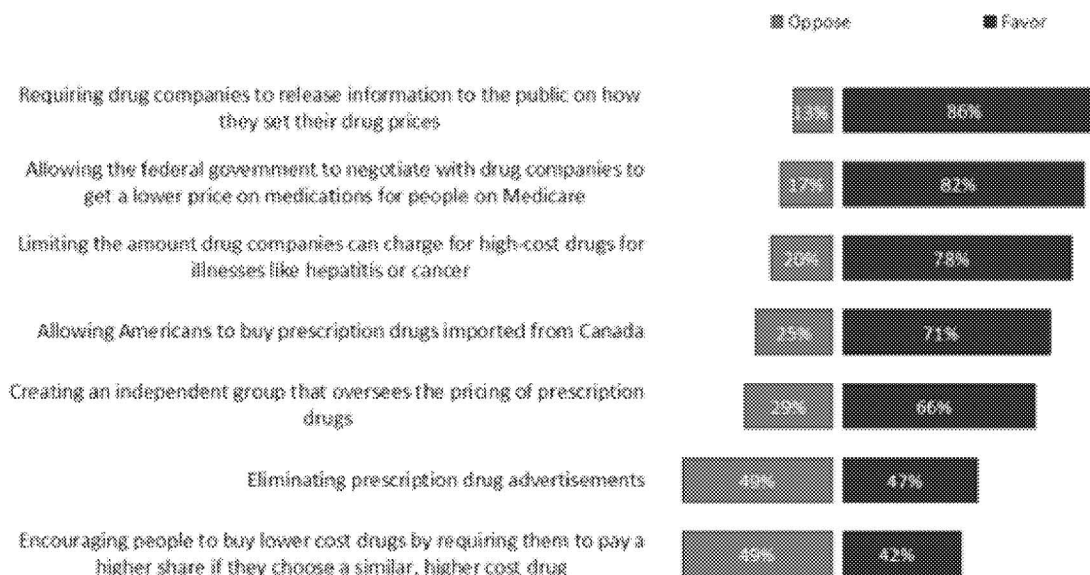
Lastly, the president to direct the Federal Trade Commission to stop drug companies' monopolistic practices, especially when drug patent holders pay generic companies to delay lower-cost alternatives to market - a practice that is sometimes called "pay for delay."

Most Americans already support strong action to rein in drug prices. The Kaiser survey showed, for example, that 82 percent of those polled support allowing the Federal government to negotiate drug prices and 71 percent support allowing Americans to purchase drugs imported for Canada.

Figure 13

Most of the Public Favors Actions to Keep Drug Costs Down

Please tell me whether you would favor or oppose the following actions to help keep prescription drug costs down...



NOTE: Question was asked of separate half sample.

SOURCE: Kaiser Family Foundation Health Tracking Poll (conducted September 14-20, 2016)



The Pocan letter is supported by a number of activist groups, including Social Security Works, People's Action, CREDO Action, and a number of other organizations. (See complete list below.)

A number of Democratic House members have signed Rep. Pocan's letter. (No Republicans have signed it, which is telling: The Bayh-Dole Act was a bipartisan piece of legislation, which seems unimaginable today.) They are listed below.

If your Representative's name isn't on the list, they have until Friday to sign it. This would be a good time to call their office and suggest that they do.

Groups Supporting the letter: CREDO Action, Social Security Works, People Demanding Action, the Other 98%, Courage Campaign, Progressive Congress, Blue America, Public Citizen, Knowledge Ecology International (KEI), Daily Kos, Public Leadership Institute, People's Action, and the Universities Allied for Essential Medicine.

(Note: I am affiliated with People's Action; Social Security Works sponsors The Zero Hour radio program on We Act Radio.)

House members who have signed the letter as of this writing:

Lloyd Doggett
 Jan Schakowsky
 Keith Ellison
 Raul Grijalva
 Nydia M. Velázquez
 Elijah E. Cummings
 Jim McDermott

Alan Lowenthal
Jared Huffman
Luis Gutiérrez
Eleanor Holmes Norton
Sam Farr
Rosa DeLauro
Gwen S. Moore
John Conyers, Jr.
Earl Blumenauer
Barbara Lee
Maxine Waters
Steve Cohen
Brenda L. Lawrence
Michelle Lujan Grisham
John Yarmuth
Donna F. Edwards
Emanuel Cleaver
Peter Welch
Richard (RJ) Eskow Host, The Zero Hour; Sr. Fellow, Campaign for America's Future

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Rep. Pocan's letter urges President Obama to "use executive action and take concrete steps" to address the drug cost crisis, and lists three tools that the president can use. The first is the Bayh-Dole Act, which gives the National Institutes of Health the power to ensure that medications that were developed at taxpayer expense are accessible to the public at affordable rates.

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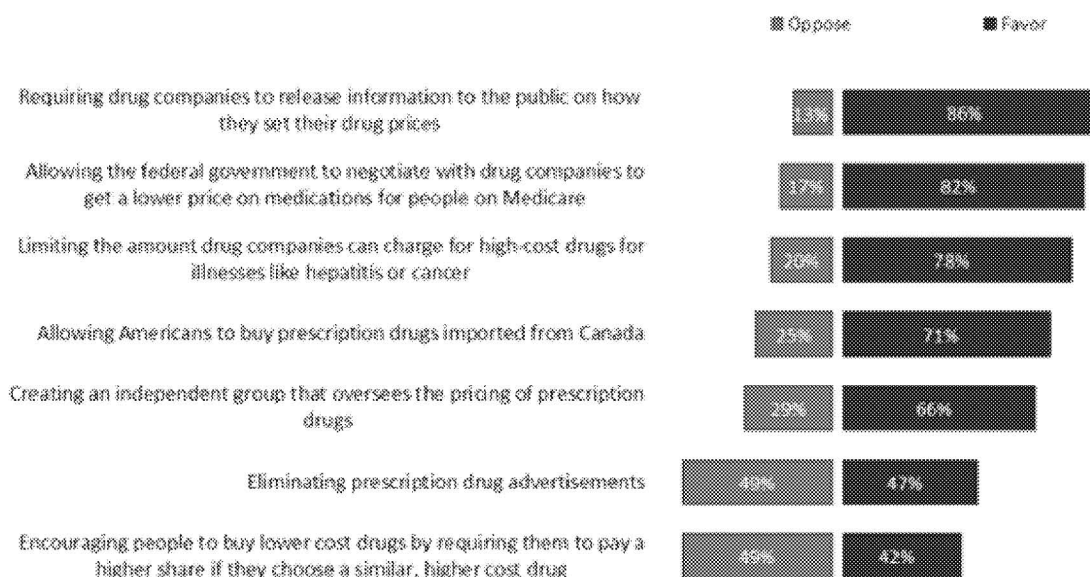
Lastly, the president to direct the Federal Trade Commission to stop drug companies' monopolistic practices, especially when drug patent holders pay generic companies to delay lower-cost alternatives to market - a practice that is sometimes called "pay for delay."

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(Note: I am affiliated with People's Action; Social Security Works sponsors The Zero Hour radio program on We Act Radio.)

House members who have signed the letter as of this writing:

Lloyd Doggett
 Jan Schakowsky
 Keith Ellison
 Raul Grijalva
 Nydia M. Velázquez
 Elijah E. Cummings
 Jim McDermott

*Alan Lowenthal
Jared Huffman
Luis Gutiérrez
Eleanor Holmes Norton
Sam Farr
Rosa DeLauro
Gwen S. Moore
John Conyers, Jr.
Earl Blumenauer
Barbara Lee
Maxine Waters
Steve Cohen
Brenda L. Lawrence
Michelle Lujan Grisham
John Yarmuth
Donna F. Edwards
Emanuel Cleaver
Peter Welch*

Follow Richard (RJ) Eskow on Twitter: www.twitter.com/rjeskow

On 10/5/2016 7:49 PM, Levis, Phil wrote:

Could you paste text? The link is not opening the website.
Phil

-----Original Message-----

From: Joe Allen [<mailto:jallen@allen-assoc.com>]

Sent: Wednesday, October 05, 2016 7:42 PM

To: Levis, Phil

Subject: House Dems urge Pres Obama to use to Bayh-Dole to control drug prices

Seen this:

[http://www.huffingtonpost.com/rj-eskow/the-president-can-act-aga b 12361118.htm](http://www.huffingtonpost.com/rj-eskow/the-president-can-act-aga-b-12361118.htm)

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/28/2017 7:36:25 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Bordine, Roger (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a44282b444584690bbbe471966f54f1f-bordinerw]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
CC: Thomas, Gina (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a7d21227e5643548f0a7c256b54f83f-gthomas]; Rogers, Karen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b23ef4ca2fa14a6eb174ee611953a396-rogersk]
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

I'm still on a conference call. I'll call everyone through skype

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 28, 2017 15:36
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>; Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Is there a call in number?

From: NIH FOIA
Sent: Monday, August 28, 2017 3:18 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>; Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

3:30pm is fine for me.

Roger Bordine
Program Assistant
Freedom of Information Office
National Institutes of Health
Building 31, Room 5B35
31 Center Drive
Bethesda, MD 20892

Phone: 301-496-5633
Fax: 301-402-4541
Roger.bordine@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 28, 2017 3:10 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>; Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Ok by me

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Monday, August 28, 2017 2:56 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Ok I have a telecon at 15:05 can we gab at 15:30?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 28, 2017 14:56
To: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

I am available the rest of today and tomorrow until 1 pm.

Mark

From: NIH FOIA
Sent: Monday, August 28, 2017 10:32 AM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Deborah.Kassilke@nih.gov; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Good Morning,

I have not yet responded, and I have cc'd Gina Thomas at OTT FOIA as well. She is handling two FOIA request cases from KEI about CRADA lists and tech transfer records.

Let me know when is best to talk with all of you so we can figure out the best way to respond soon.

Thanks.

Roger Bordine

Program Assistant
Freedom of Information Office
National Institutes of Health
Building 31, Room 5B35
31 Center Drive
Bethesda, MD 20892

Phone: 301-496-5633
Fax: 301-402-4541
Roger.bordine@nih.gov



From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Monday, August 28, 2017 9:52 AM
To: Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Cc: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Deborah.Kassilke@nih.gov; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

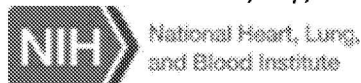
Roger –

b5

b5

Thank you!!

Michael A. Shmilovich, Esq., CLP



Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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From: jamespackardlove@gmail.com [<mailto:jamespackardlove@gmail.com>] **On Behalf Of** Jamie Love
Sent: Monday, August 28, 2017 08:28
To: Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>

REL0000024138

Cc: Claire Cassedy <claire.cassedy@keionline.org>; NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Deborah.Kassilke@nih.gov; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Dear Roger Bordine,

I am attaching some correspondence I have had the NIH over the issue of CRADAs. When we respond to an NIH request for comments on an exclusive license, we often ask for the CRADA, if any, associated with the license. For example, recently we requested the CRADA associated with the miRecule CRADA, which involves a recent former NIH employee. Typically, as in the case of MiRecule, the NIH licensing officials refuses to give us a copy of the CRADA, claiming it is confidential. We both know that the CRADA document is in fact subject to FOIA, but FOIA takes a long time, can will not be processed before the comment period closes.

When we asked the Office of the Director for a list of all CRADA agreements earlier this year, we were told that the NIH would not provide such a list, because the information was in a computer database and the NIH was not required to create the list from the database under FOIA. We noted at the time that this would force us to FOIA all of the CRADAs, which we thought would be a waste of everyone's time, an opinion that you seemed to share.

Why doesn't the NIH do what some other federal agencies do and list the CRADAs, all of them, on the NIH web page, to enhance the transparency of the licensing and technology transfer operations?

In any event, please decide if the NIH wants to provide a list of the CRADAs or not, and if we have to sue to get copies if you won't in fact provide such a list.

The NIH knows full well the Congress, the press, academic researchers, taxpayer and patient advocacy groups all want to have more transparency of NIH technology transfer activities. The continual stonewalling of legitimate requests for public documents is inappropriate for an agency like the NIH that manages billions of taxpayer dollars to address important health issues, and where the pricing of NIH funded products is a major concern.

In the meantime, please provide KEI with a copy of the miRecule CRADA, and the list of the CRADAs, asap.

James Love
Knowledge Ecology International

Attached are portions of some previous correspondence with the NIH.

----- Forwarded message -----

From: **NIH FOIA** <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>

Date: Wed, Aug 16, 2017 at 5:15 PM

Subject: RE: Request FOIA Request Re: CRADAs Executed 2010-2017

To: Claire Cassedy <claire.cassedy@keionline.org>

Cc: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>

Good Afternoon,

Thank you for your NIH FOIA request.

REL0000024138

Upon reading your request, it appears as though you are asking for all CRADAs from the NIH between 2010-2017, and as it stands, that aspect of your request is too broad and would involve searching records from of all of the 27 institutes and centers at the NIH.

Searching for this many records, and the review efforts afterwards, would put an undue burden on Federal Government resources, as stipulated in the FOIA, and as such, requires you to narrow the scope of your request.

It is estimated that, within your requested timeframe, there would be hundreds of CRADAs across the NIH's institutes, and if you would like to submit a new/revised request detailing a smaller number of specifically named/individual CRADAs, you are more than welcome to request those records. If not, and you would rather request just a list of CRADAs and not the CRADA records themselves, you may do that instead.

Please let us know if you would like to withdraw this initial request in favor of submitting a new request for clarified/named records.

Thank you, and please let us know if you have any questions.

Roger Bordine

Program Assistant

Freedom of Information Office

National Institutes of Health

Building 31, Room 5B35

31 Center Drive

Bethesda, MD 20892

Phone: 301-496-5633

Fax: 301-402-4541

Roger.bordine@nih.gov

----- Forwarded message -----

From: **James Love** <jamespackardlove@gmail.com>

Date: Thu, Jan 19, 2017 at 7:34 PM

Subject: Re: Your requests for information from NIH OTT

To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@od.nih.gov>

Cc: "Kassilke, Deborah (NIH/OD) [E]" <deborah.kassilke@nih.gov>, "claire.cassedy@keionline.org" <claire.cassedy@keionline.org>

We can't FOIA a database or require records be generated under FOIA. We can FOIA every CRADA, which is what we are going to be forced to do.

But if we knew what records were in the database, a query might save everyone a lot of time.

On Fri, Jan 20, 2017 at 1:07 AM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@od.nih.gov> wrote:

There is no "list" but we do have a database with CRADA and license information.

From: James Love [mailto:jamespackardlove@gmail.com]

Sent: Thursday, January 19, 2017 7:01 PM

To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>

Cc: claire.cassedy@keionline.org; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

Subject: Re: Your requests for information from NIH OTT

These are the types of data that make it hard to believe you don't have registry or list of the CRADAs.

<https://www.ott.nih.gov/tt-metrics/crada-metrics>

On Fri, Jan 20, 2017 at 12:56 AM, James Love <jamespackardlove@gmail.com> wrote:

Thank you.

We do note that the NIH is able to report the total number of CRADAs in any given year, and also that that number is quite a bit smaller than the number of CRADAs noticed in the federal register.

For number of CRADAs, <https://www.ott.nih.gov/ott-statistics>

We are mostly interested in the Standard CRADAs.

We thought if the NIH could provide a count of the number of CRADAs, they must have a registry or list or database that lists the CRADAs, with the name of the CRADA partner and the purpose of the CRADA.

We were surprised when we were told that no such lists exist.

The CRADAs mentioned in the annual reports do not seem inclusive of all CRADAs in a given year.

For example:

In FY15, NIH Institutes executed 5,826 of these collaboration and transfer agreements, including 101 new Cooperative Research and Development Agreements (CRADAs).

I don't think there are 101 CRADAs listed in the annual report, or even the 73 for Standard CRADAs.

So, while the Annual report is useful and interesting, we still don't know who is getting the standard CRADAs.

Also, does the NIH issue exclusive licenses under the CRADAs that are not noticed in the federal register? We were told that the NIH practice was to not provide public notice and comment on all CRADAs and that public notice and comment is not available for all exclusive licenses from CRADAs.

Jamie

On Fri, Jan 20, 2017 at 12:26 AM, Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov> wrote:

Mr. Love –

Recently your office contact me and two other employees in my office with questions concerning royalty payments, the use of the Federal Registry in tracking NIH CRADAs, and a request for information on the process by which the NIH enters into a CRADA with an industry collaborator. I am aware that Mark Rohrbaugh (cc'd) spoke directly with Claire Cassidy to discuss many of the CRADA related process components including the use of

Federal Register notices and how IP is addressed in a CRADA. If you still have questions regarding the use of CRADAs at NIH, we can certainly schedule another call with you.

I confirmed that the NIH FOIA office is still working on a FOIA request for you concerning royalty payment information. They apologize for the delay, but the FOIA office is short staffed at this time and they are working diligently to hire and train new staff. We just last week brought in an Acting Director for the FOIA office, Katherine Uhl, who is on detail to us from the FDA. She is working diligently to keep the plates spinning and asked that I relay to you they are working on the request. Ms. Uhl invites you to contact her office for a status of your FOIA request if you so desire; that number is 301-496-5633.

I hope that you are aware that our annual reports and statistics can be found on our website in the "MEDIA Room" tab; they may be helpful to you.

Please let me know if you would like another call scheduled with Mark and me; we will gladly set something up.

Deb

Deborah Kassilke

Director, Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

E-Mail:

Deborah.Kassilke@nih.gov

Phone: 301-435-5294

Cell:

b6



From: Claire Cassedy [mailto:claire.cassedy@keionline.org]
Sent: Tuesday, August 15, 2017 11:38 AM
To: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>
Subject: Request FOIA Request Re: CRADAs Executed 2010-2017

Dear FOIA Officer,

Please find attached a Freedom of Information Act request from Knowledge Ecology International regarding Cooperative Research and Development Agreements executed by the NIH from 2010 to 2017. Thank you in advance for your attention to this request.

Sincerely,

Claire Cassedy

----- Forwarded message -----

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Date: Fri, Aug 18, 2017 at 10:34 AM
Subject: FW: miRecule CRADA
To: "jamespackardlove@gmail.com" <jamespackardlove@gmail.com>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutcha@nhlbi.nih.gov>, "Bailey, Brian (NIH/NHLBI) [E]" <bbailey@nhlbi.nih.gov>

Jamie – All scientific, business and financial information pertaining to the CRADA between MiRecule and NIDCD other than what has already been made public by either by publication, published patent applications or other public disclosures, is strictly confidential. As such, we cannot provide you with a copy of that agreement.

Regards,

Michael A. Shmilovich, Esq., CLP

22 August 2017
James Packard Love

REL0000024138

Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

<http://keionline.org>

Work: +1.202.332.2670; Mobile: +1.202.361.3040

james.love@keionline.org

IN RE: 82 Fed. Reg. 36809 (August 7, 2017), "Prospective Grant of Exclusive Patent License: MicroRNA therapeutics for treating squamous cell carcinomas" to miRecule, Inc.

Dear Mr. Love:

....

Dr. Saleh will have direct participation in the research under his company's Cooperative Research and Development Agreement (CRADA) with the National Institute on Deafness and Other Communication Disorders (NIDCD) in order to advance the technology since a positive research outcome under the CRADA is one step closer to the development of a successful therapeutic to at least one squamous cell carcinoma. With respect to your request for various reports including CRADA documents, it is not consistent with our mission to create reports requested by the public and the proprietary content of the agreement governing the CRADA between the NIDCD is strictly confidential. In summary, the CRADA research plan sets forth a joint effort between miRecule and NIDCD to develop chemically modified mimic or mimetic microRNAs that are stable and less susceptible to nuclease degradation than previously identified microRNAs and that serve as therapeutics for cancer when delivered using tumor targeted nanoparticles. The CRADA will test these microRNAs in animal cancer models to evaluate their efficacy and the pharmaceutical properties of candidate formulations.

If your organization requests more documentation, such requests should be filed under the Freedom of Information Act. The webpage for the NIH FOIA Office provides more information on filing requests <http://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedominformation-act-office/submitting-foia-requests>.

Michael A. Shmilovich, Esq., CLP

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: Joe Allen [jallen@allen-assoc.com]
Sent: 6/15/2017 8:38:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Stevens, Ashley J [astevens@bu.edu]; Robert Hardy [RHardy@COGR.edu]
Subject: Re: Lawmakers ask U.S. Army to hold a hearing on Zika vaccine licensing

Here's FiercePharma's story:

Lawmakers in hard-hit Florida want public hearing in Sanofi Zika vaccine scuffle

by Eric Sagonowsky |
Jun 15, 2017 8:00am

Having seen Zika's devastating effects reach Florida residents, a bipartisan group of lawmakers in the state is urging the Army to pump the brakes on its exclusive vaccine license to Sanofi.

In letters to acting Army Secretary Robert Speer, nine members of the House of Representatives from the state and Sen. Bill Nelson have castigated the proposed vaccine license, questioning why the partners can't include a fair pricing assurance. The House members are requesting that the license be delayed until officials can hold a public hearing on the plan.

RELATED: [Sanofi's Zika-shot pricing dust-up highlights a divide over taxpayer-backed vaccine R&D](#)

For his part, Sen. Nelson noted that more than 1,400 cases of Zika have been documented in Florida. He [wrote](#) (PDF) that a “failure to limit the vaccine’s market price could make it inaccessible to thousands of Floridians who need it.” Nonprofit Knowledge Ecology International (KEI) posted the letters on its website Wednesday.

The Army and reportedly Sanofi itself have rejected calls for pricing assurances on the planned license, first announced late last year. Their refusal has angered politicians and public watchdog groups who have pointed out that the vaccine was developed with funds from U.S. taxpayers.

In response to the requests, the Army said it simply can't enforce future vaccine prices. Sanofi has said that the terms of the license are still under negotiation.

KEI was among the first to protest the proposed license, kicking off a campaign that's gained a great deal of steam in recent months. Sen. Bernie Sanders wrote a New York Times op-ed requesting the Trump administration call the deal off, and Sanofi R&D head Elias Zerhouni defended his company in the same newspaper.

RELATED: [Lawmakers decry Army's planned Zika vaccine license to Sanofi](#)

Zerhouni pointed out that Sanofi wouldn't be getting something for nothing in the deal and that the drugmaker would have to pay "significant" milestone and royalty payments if the partners are able to develop a successful vaccine. Before the Florida lawmakers wrote to protest the deal, a separate group of 11 Democrats urged against the license back in February.

On Wednesday, KEI's counsel for policy and legal affairs, Andrew Goldman, said in a written statement that the new letters "highlight the absurdity of paying for virtually all of the R&D for the vaccine, giving a French company a monopoly until 2036, and not having any conditions on the price before signing the license."

The U.S. government is also partnered with GlaxoSmithKline and Takeda on different Zika vaccine approaches, and the proposed license to Sanofi would not prohibit other companies from bringing vaccines to market and competing on price.

"Whether or not the agreement with WRAIR is exclusive or non-exclusive, the license does not prevent other companies from pursuing vaccine candidates based on alternative technologies which have the potential to be more viable than this one," a Sanofi spokesperson said on Wednesday. "There is a very strong likelihood there will be a competitive Zika vaccine marketplace with 32 Zika vaccines in early development. Many of these other companies are also receiving funding from the U.S. government."

RELATED: [Sanofi executive lays out case for taxpayer funding—and exclusive licensing—on Zika vaccine R&D](#)

Further, it's in the "public-health interest for Sanofi to price this and other vaccines in a way that will facilitate access to and usage of a preventative vaccine," she said.

The Army is set to decide on the license by the fall, [according](#) to the Miami Herald. Its press office didn't immediately respond to a request for comment on the letters.

Sanofi partnered with the U.S. Army last summer and has since won \$43 million in government funds to support the project. Another \$130 million could be awarded for future work. Army scientists originally developed the candidate. Market-watchers have [predicted](#) the Zika vaccine market could be worth \$1 billion per year or more.

[Facebook](#) [Twitter](#) [LinkedIn](#) [Email](#)

On 6/14/2017 3:22 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

FYI: <https://www.statnews.com/pharmalot/2017/06/14/lawmakers-army-zika-vaccine/>. NIH is mentioned at the end of the article.

Lawmakers ask U.S. Army to hold a hearing on Zika vaccine licensing

By ED SILVERMAN [@Pharmalot](#)
JUNE 14, 2017

A group of Florida lawmakers is urging the U.S. Army to hold a hearing on its plan to give Sanofi an exclusive license to develop a Zika virus vaccine, a move that has raised concerns the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

In a June 13 [letter](#), eight U.S. House Democrats and one Republican expressed concern about the “potential for monopolistic practices that would, effectively, keep this life-saving vaccine out of reach for far too many of our constituents.” At the same time, U.S. Sen. Bill Nelson, who is also a Democrat, sent his own [letter](#) in which he urged the Army to limit the price for the vaccine.

Both missives noted that Sanofi, which is one of the world’s largest vaccine makers, has already won a \$43 million government grant and stands to receive another \$130 million to run late-stage trials. Consequently, the representatives argued that awarding an exclusive license to the company would add “insult to injury,” and they want the Army to explain how such a license is reasonable or necessary.

This the second time in recent weeks that lawmakers from a Gulf state have decried plans for an exclusive license. Last month, Louisiana Gov. John Edwards warned Acting U.S. Army Secretary Robert Speer that if the mosquito-borne virus spreads, the possibility of monopoly pricing “could cripple state budgets and threaten public health.”

The letters may ratchet up the pressure on the Army to change course amid cries from still other lawmakers and consumer advocates to demand that Sanofi agree to some kind of pricing agreement as part of any licensing deal. As we reported recently, however, the company in April [rejected such a request](#) from the Army, although overall licensing talks are still under way.

We asked the Army if a hearing will be scheduled and we will update you accordingly.

The episode highlights a growing debate about the extent to which drug makers should be allowed to benefit from products that are developed — at least in part — with taxpayer funds. In this instance, the lawmakers and consumer advocates are concerned over speculation that, if the virus spread quickly, Sanofi will have a lock on a potentially lucrative market.

One group, Knowledge Ecology International, argued Sanofi cannot be trusted and pointed to pricing for its Aubagio multiple sclerosis drug. Americans using a coupon can pay about \$6,100 for a month’s supply — which is seven times more than patients pay in France and at least four times the price in the UK, Ireland, and Australia. Sanofi countered that prices vary due to circumstances in each country.

The advocacy group has also made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit. But in a recent [letter](#) to U.S. Sen. Bernie Sanders, Robert Speer, noted that only Sanofi was “willing to license” this specific discovery, prompting concern that the Army is unwilling to push the company about pricing over fears it may walk away.

For its part, Sanofi has said that a price has not yet been set, but one executive maintained that royalties would be paid. Meanwhile, in a May 22 letter to a Congressional subcommittee, another Sanofi executive insisted the company is not pursuing the project

based on a “commercial return” and intends to price the vaccine in order to “facilitate access” in the interest of public health.

Moreover, Adam Gluck, who heads U.S. government relations at Sanofi, noted that the company delayed other R&D programs to speed development of the vaccine out of a “sense of corporate responsibility” to address a potential public health crisis. But he also warned that, “given the high-risk nature of vaccine development unpredictability for diseases like Zika, if the U.S. government changes its historic approach to licensing terms, it could undermine the intent of these types of collaborations.”

His language raised debate over whether the federal government should reinstate language in research agreements that contain “reasonable pricing.” This requirement was removed by the U.S. National Institutes of Health in 1995 over concerns that such clauses would be seen by industry as a “restraint” on new product development.

--

Joseph P. Allen
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From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 6/26/2019 4:20:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Pazman, Cecilia (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bf35741501e247d887acd224eaf9d679-pazmance]
Subject: FW: Additional inquiry regarding 84 FR 28063 Doc 2019-12708, "Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors"

Mark – please review my proposed response to Luis from KEI.

b5

b5

From: Luis Gil Abinader <luis.gil.abinader@keionline.org>

Sent: Wednesday, June 26, 2019 11:04

To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>

Cc: Jamie Love <james.love@keionline.org>; claire.cassedy <claire.cassedy@keionline.org>

Subject: Additional inquiry regarding 84 FR 28063 Doc 2019-12708, "Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors"

Dear Mr. Shmilovich,

I am writing in reference to the Federal Register notice (84 FR 28063 Doc 2019-12708) regarding, "Prospective Grant of Exclusive Patent License: Lutetium-177 Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors," for which you are listed as the contact for inquiries. Thank you for your previous response to my colleague Claire Cassidy. We have additional questions about the proposed license.

1. Does the license includes the Singapore patent application 11201809982R, which entered the national phase via the PCT procedure PCT/US2017/031696?
2. Is <http://www.mtarget.com/SFNT.html> the website of the prospective licensee?
3. The Federal Register notice 84 FR 28063 states that the NIH is contemplating amending "an existing license". Is the "existing license" the prospective exclusive license described in the Federal Register notice 83 FR 35663, published on July 27, 2018?
4. Was the license proposed in the Federal Register notice 83 FR 35663 executed?
5. How will the exclusive license proposed in the Federal Register notice 84 FR 28063 amend the previous license described in the Federal Register notice 83 FR 35663?
6. What is the rationale for granting additional exclusive rights to a company that presumably has outstanding obligations under a previous license?
7. A clinicaltrials.gov search for the term "DOTA-EB-TATE" returns two phase I clinical trials, NCT03308682 and NCT03478358, both related to neuroendocrine tumors. These trials were co-sponsored by the Peking Union Medical College Hospital and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), according to clinicaltrials.gov. Are these trials related to the proposed exclusive license?
8. Based on our own research, our understanding is that the invention covered in the proposed license, 177Lu-DOTA-EBTATE, has more favorable pharmacokinetics compared to 177Lu-DOTATATE, a therapy for neuroendocrine tumors recently approved by the FDA and marketed under the brand name Lutathera. Is this correct?

Thank you in advance for your assistance,

Luis Gil Abinader

REL0000024141

From: Koniges, Ursula (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D5AE2C3139654BC0B9B95718D516310B-KONIGESUM]
Sent: 4/4/2018 4:39:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Dodson, Sara (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=985a956eaa0d4945bdcfd8ea30947d68-dodsonse]
Subject: RE: Opioids – KEI Requests White House Sidestep Naloxone Patents
Attachments: Opioids_KEI_StatPlus.pdf; Conway-Carrol-KEI-1498-Evzio-29mar2018.pdf

NIH Library just shared the Stat+ article (attached) related to the KEI White House request (also attached). Article text below:

White House is urged to sidestep patents on opioid overdose treatment

By ED SILVERMAN / April 2, 2018

The White House is being urged to sidestep patents on a high-priced opioid overdose antidote as one way to stem the rising cost of combating the opioid crisis.

In a [letter](#)¹ sent last Thursday, an advocacy group argues the White House should use a little-known [federal law](#)² that would permit the government to take title to patents on Evzio. This is a decades-old version of naloxone, which is widely used to reverse the effect of opioid and heroin overdoses.

A package of two Evzio auto-injectors at 0.4 mg dosing, which is sold by Kaleo Pharma, has a list — or wholesale — price of \$3,750, according to Truven Health Analytics, an IBM Watson business. The price has jumped from \$575 when the product won regulatory approval in 2014. Meanwhile, a 2 mg dose package has a list price of \$4,100. Several federal agencies, in fact, have recommended increasing access to naloxone, especially for prescription-opioid users, and the high prices have prompted [scrutiny](#)³ from congressional lawmakers. Meanwhile, the

pricing has also strained municipal government budgets because first responders increasingly rely on the product in the wake of the growing number of opioid overdoses around the country.

“A consequence of the high price for the Evzio device is a combination of fiscal strain on the local budgets for first responders, or worse, a lack of access to the technology when it is needed,” Knowledge Ecology International, the advocacy group, wrote to the White House. “The federal government can take action to moderate the price and to expand access to these life-saving technologies.”

So the group is urging the White House to consider using a law that dates back to 1910 and resembles eminent domain: The federal government could use a patented invention without permission, and a drug maker could demand a “reasonable” compensation — such as royalties — but cannot stop the government from taking such a step.

“In this case, the federal government is leading an effort to address the opioid epidemic and searching for ways to save lives. One concrete step would be to notify Kaleo that, unless the company rolls back its 500 percent increased price for Evzio, the U.S. will grant compulsory licenses on all of its patents, and authorize local responders of all types to acquire less expensive versions,” the group wrote.

“By beginning the process of overriding the exclusive rights in the Evzio patents, Kaleo will have a strong incentive to avoid the compulsory license, and the Trump Administration will have an opportunity to lower the prices, and consequently save lives,” KEI argued. “To do nothing is the worst option, since the current outcome is unacceptably bad for first responders and patients.”

This approach has been floated a few times over the past year as government agencies grapple with rising prices for some medicines. Last month, a group of congressional Democrats urged the Department of Health and Human Services to tap the law in order to sidestep patents on hepatitis C medicines in hopes that lower-cost generics could be manufactured.

As for Kaleo, the company sent us a statement saying it agrees that “the out-of-pocket cost to the patient can be a major barrier to access to naloxone,” and pointed to a scheme in which patients with commercial insurance and a prescription can pay nothing. Those patients who have no government or commercial insurance and have a household income of less than \$100,000, would also pay nothing. For those paying cash, the outlay would be \$360, the company noted last year.

The company has argued that the higher prices are needed to ensure most patients can obtain the product at no cost. Drug makers regularly offer rebates and discounts, so payers frequently pay much less, but Kaleo is counting on enough payers to cover Evzio in order to make a profit, while also underwriting the cost for people who cannot afford its medicine.

The drug maker also maintained that since launching its enhanced patient access program in 2016, more Americans can obtain naloxone for \$0 than ever before. As for the cost to municipal governments. The company replied that “no first responder organization has ever purchased Evzio at the list price. Instead, we have donated more than 300,000 Evzio auto-injectors to hundreds of first responder agencies, public health departments, and qualifying non-profit community groups across 35 states.”

In response KEI’s Jamie Love had this to say: “Kaleo is involved in price gouging, no matter how they spin it. They increased the price by 500 percent overnight to exploit a public health emergency. The fact that they have donations out there is irrelevant, as there are individuals and institutions who cannot access this treatment because of the price. We always hear people complaining about high prices but we don’t see much action. One thing we’ve been trying to focus on at KEI is the fact that in many cases, the government has leverage, and this is one of those cases.”

From: Koniges, Ursula (NIH/OD) [E]

Sent: Tuesday, April 03, 2018 9:37 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Dodson, Sara (NIH/OD) [E] <sara.dodson@nih.gov>

Subject: Opioids – KEI Requests White House Sidestep Naloxone Patents

Latest from KEI via [STAT Plus](#). The letter from KEI to the White House at this [link](#) and attached. I’ll request the article from the NIH Library, and I’ll share it once I receive it.

Group Asks White House To Take Over Patents For Opioid Overdose

Reversal Drug. STAT Plus (4/2, Silverman, Subscription Publication, 32K) reports the advocacy group Knowledge Ecology International wrote a letter (PDF) to the White House urging officials to “sidestep patents” on Evzio’s “decades-old version of naloxone, which is widely used to reverse the effect of opioid and heroin overdoses.” A package of two doses costs \$3,750 – up from \$575 when the medicine won FDA approval in 2014. The group invokes a 1910 law and which says that the federal government “could use a patented invention without permission, and a drug maker could demand a ‘reasonable’ compensation – such as royalties – but cannot stop the government from taking such a step,” according to STAT.

White House is urged to sidestep patents on opioid overdose treatment

By ED SILVERMAN @PharmaLot / April 2, 2018



John Minchillo/AP

The White House is being urged to sidestep patents on a high-priced opioid overdose antidote as one way to stem the rising cost of combating the opioid crisis.

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pricing has also strained municipal government budgets because first responders increasingly rely on the product in the wake of the growing number of opioid overdoses around the country.

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“In this case, the federal government is leading an effort to address the opioid epidemic and searching for ways to save lives. One concrete step would be to notify Kaleo that, unless the company rolls back its 500 percent increased price for Evzio, the U.S. will grant compulsory licenses on all of its patents, and authorize local responders of all types to acquire less expensive versions,” the group wrote.

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About the Author



Ed Silverman

Pharmalot Columnist, Senior Writer

Ed covers the pharmaceutical industry.

ed.silverman@statnews.com

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March 29, 2018

Ms. Kellyanne Conway
Counselor to the President

Mr. James Carroll
Acting Director, Office of National Drug Control Policy
oipl@ondcp.eop.gov

Dear Ms. Conway and Mr. Carroll;

We are writing to ask that the Trump Administration use its authority under 28 USC § 1498(a) to authorize third parties to manufacture and sell affordable versions of two devices which deliver naloxone to treat persons suffering from an opioid overdose. This statute allows the federal government to authorize third parties to use patented inventions without the permission of the patent holder, if the use is by or for the federal government.

As you know, opioid overdose deaths in the United States have been rising throughout the past decades, and represent a significant public health concern across the country. Data from 2016, the most recent year for which it is available, showed that opioids were involved in 42,249 deaths. It is critical that first responders have the necessary tools at their disposal to save the lives of overdose victims before it is too late, and that friends, family, and colleagues are also able to access the devices that can save the life of a loved one.

Naloxone was first approved by the FDA as a priority drug on April 13, 1971, nearly 47 years ago, and the drug itself is not expensive. However, first responders prefer to use the drug in connection with delivery mechanisms that make its use safer and more effective, and these particular mechanisms are more useful for non-medical personnel. These safer and more effective devices are very expensive.

The two leading technologies are the Evzio and Narcan devices.

Narcan, which provides 4mg of naloxone through a nasal spray and is marketed by Adapt Pharma, has a price of \$150 for a set of two single use nasal spray devices. Some patients need several doses. Narcan is currently protected by seven patents, which are assigned to Adapt Pharma Limited, Opiant Pharmaceuticals, and Lightlake Therapeutics.

Evzio is an auto-injector of naloxone marketed by kaléo Inc. (Until 2014, kaléo was named Intelliject). This is the only naloxone auto-injector currently approved by the FDA, and provides a rapid dose of 2 mg of naloxone, and features both written and audio instructions for users, making it a useful tool not only for police or paramedics who may respond first to a call, but also for the family and friends of those who may suffer an overdose. Kaléo has filed 25 patents in the FDA Orange Book for Evzio, including several patents with similar names and the same priority dates, all listing two brothers, Evan and Eric Edwards, among the inventors.

Kaléo first put Evzio on the market in 2014 at a price of \$690 for a set of two auto-injectors. The product, also known as intramuscular naloxone, is intended for single use, and it is not uncommon for some overdose patients to require multiple doses for revival. Kaléo has capitalized on the worsening epidemic, raising the price of Evzio over 500 percent, to a current list price of \$4,500.

A consequence of the high price for the Evzio device is a combination of fiscal strain on the local budgets for first responders, or worse, a lack of access to the technology when it is needed.¹

The federal government can take action to moderate the price and to expand access to these life saving technologies.

The United States Government can authorize third parties to use any patents without the permission of the patent holder, when the use is by or for the federal government. In this case, the federal government is leading an effort to address the opioid epidemic and searching for ways to save lives. One concrete step would be to notify kaléo that unless the company rolls back its 500 percent increased price for Evzio, the U.S. will grant compulsory licenses on all of its patents, and authorize local responders of all types of to acquire less expensive versions

¹ There have been numerous instances in which the high cost of opioid-reversal medication has led to calls for rationing from local governments faced with constraints on first responder budgets. In June of 2017, the city council in Middletown, Ohio, discussed a three strikes policy for patients who overdose repeatedly, at which point first responders would no longer revive them. A few weeks later, a county commissioner in Martin County, Florida, discussed a similar proposal. The prohibitive cost of naloxone, a generic drug, completely due to patents on delivery devices, has raised concerns in Philadelphia, Baltimore, Allegany County Maryland, Cincinnati, and in countless other towns and counties across the country. For further reading, see:

Cleve R. Wootson Jr, "[One politician's solution to the overdose problem: Let addicts die](#)" *The Washington Post*, June 30, 2017.

Julius Whigham II, "[Should OD rescues be limited? Questions rise as Narcan's cost soars](#)" *Palm Beach Post*, July 20, 2017.

Christopher Moraff, "[Narcan Prices are Skyrocketing and Cities are Begging for Help to Buy It](#)" *The Daily Beast*, September 8, 2016.

Meredith Cohn, "[Cost of overdose drug could hamper access in Maryland and elsewhere](#)" *The Baltimore Sun*, February 13, 2017.

Heather Wolford, "[Decreased revenue, increased Narcan fee, shoot up cost of Allegany County EMS overdose calls](#)" *Cumberland Times-News*, September 14, 2017.

T.J. Parker, "[Cost of Narcan taking a bite out of emergency responders' budgets](#)" *WCPO Cincinnati*, April 13, 2017.

from new manufacturers. Even though it will take awhile for the competitors to enter the market, the compulsory license on the patents will shorten the effective monopoly, and that will give the federal government leverage to negotiate lower prices.

The legal basis for the compulsory license is 28 U.S.C. § 1498, which states:

(a) Whenever an invention described in and covered by a patent of the United States is used or manufactured by or for the United States without license of the owner thereof or lawful right to use or manufacture the same, the owner's remedy shall be by action against the United States in the United States Court of Federal Claims for the recovery of his reasonable and entire compensation for such use and manufacture.

And, for clarity, the statute also says:

For the purposes of this section, the use or manufacture of an invention described in and covered by a patent of the United States by a contractor, a subcontractor, or any person, firm, or corporation for the Government and with the authorization or consent of the Government, shall be construed as use or manufacture for the United States.

Government invocation of 28 U.S.C. § 1498 in order to improve access to overdose reversal treatment would be a strong, impactful action to correct the price gouging that these companies are engaging in.

The principal objection to the use of 28 U.S.C. § 1498 for the compulsory licensing of patents that is most often raised concerns the uncertainty regarding the compensation to the patent holder, a view expressed in 2002 by Alex Azar in connection with efforts to obtain sufficient quantities of ciprofloxacin for a stockpile.² We believe § 1498 is particularly appropriate for cases where the federal government has rights in some but not all relevant patents (as may be the case for Gilead's sofosbuvir, per KEI's recent letter to Secretary Azar on the issue of undisclosed federal funding³), where the use is for something that would not normally constitute a market for a product (e.g., the creation of a stockpile of ciprofloxacin to protect against an antibiotic resistant strain of anthrax poisoning in the wake of possible terror attack), or to remedy an excessive and unjustified price hike, which is the case for Evzio.

In any case, by authorizing third parties to make Evzio-like devices today, the issue of the compensation to the patent holders can be resolved before decisions have to be made on purchases. The court-ordered compensation is expected to be considerably less than the price kaléo is charging for the product, particularly if the court applies a conventional single-digit royalty against the older price or the competing device price. By framing the decision as one to

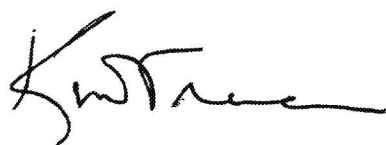
² Alex Azar II. CIPRO: Good Deal, Good Policy; Letters, The American Lawyer, April, 2002.

³ <https://www.keionline.org/27205>

remedy an excessive and unjustified price hike and to expand access for first responders, the government is also providing a context that will make it less likely that the court will set a royalty that frustrates the government's policy objective.

By beginning the process of overriding the exclusive rights in the Evzio patents, kaléo will have a strong incentive to avoid the compulsory license, and the Trump Administration will have an opportunity to lower the prices, and consequently save lives. To do nothing is the worst option, since the current outcome is unacceptably bad for first responders and patients.

We request a meeting to discuss this proposal in further detail.

A handwritten signature in black ink, appearing to read 'Kim Treanor', with a stylized, cursive script.

Kim Treanor
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
202-332-2670
kim.treanor@keionline.org

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 8/14/2018 1:52:23 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
Subject: FW: Request for Call Regarding May 18th Letter on Non-disclosure of NIH Funding of Vizamyl Patents
Attachments: Azar-KEI-CoverLetter-Vizamyl-patents-18May2018.pdf; Vizamyl-patent-memo-UofPittsburgh-Klunk-Mathis-Wang-18May2018.pdf; KEI-Briefing-Note-2018-1.pdf

From: Claire Cassedy <claire.cassedy@keionline.org>
Sent: Tuesday, August 07, 2018 2:16 PM
To: NIH OTT (NIH/OD) <NIHOTT@mail.nih.gov>; secretary@hhs.gov; Collins, Francis (NIH/OD) [E] <collinsf@od.nih.gov>; Levinson, Dan R (OIG/IO) <dan.levinson@oig.hhs.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: James Love <james.love@keionline.org>; Merith Basey <merith@essentialmedicine.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>
Subject: Request for Call Regarding May 18th Letter on Non-disclosure of NIH Funding of Vizamyl Patents

To Whom It May Concern:

On May 18, 2018 KEI requested that the Department of Health and Human Services (HHS) investigate the failure to disclose National Institutes of Health (NIH) funding in four patents on Vizamyl (INN flutemetamol F 18), which is used to evaluate possible cases of Alzheimer's disease and other causes of cognitive decline. Attached is a copy of the request and related attachments.

The patents in question are assigned to the University of Pittsburgh, and all list the same three inventors, William Klunk, Chester A. Mathis, Jr., and Yanming Wang. As the request details, in published papers that describe the inventions in Vizamyl, the inventors/authors acknowledge NIH and Department of Energy (DOE) funding of their work, but did not report the grants on the patents themselves, and the patents do not appear in the NIH RePORTER database.

KEI has asked HHS, as a remedy to this failure to disclose federal funding, to take title to the patents (a remedy available to the government in cases of non-disclosure of federal funding, as laid out in the Bayh-Dole Act).

We would like to request a phone call to discuss this outstanding request to investigate. Please let us know who the appropriate contact would be on this issue and what dates/times they would be available for a call. Thank you in advance for your time and attention to this issue.

Sincerely,
Claire Cassedy

--
Claire Cassedy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

On Fri, May 18, 2018 at 1:07 PM, James Love <james.love@keionline.org> wrote:

REL0000024145

Attached is a coverletter, memo and attachment concerning the failure of the University of Pittsburgh to disclose NIH funding in 4 patented inventions on the drug Vizamyl.

James Love

James Love, Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love



May 18, 2018

The Honorable Alex Azar
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Via email: secretary@hhs.gov

Re: Investigation into the failure disclose NIH funding in inventions patented by the University of Pittsburgh for flutemetamol F 18),

Dear Secretary Azar:

We are writing to ask the Department of Health and Human Services (HHS) to investigate and if applicable, to remedy a failure to disclose National Institutes of Health (NIH) funding in four inventions patented by the University of Pittsburgh. The four inventions are identified in the FDA Orange Book as patents for Vizamyl (INN flutemetamol F 18), used to evaluate possible cases of Alzheimer's disease or other causes of cognitive decline. Access to the tests is currently restricted, including restrictions on reimbursements by Medicare.

Knowledge Ecology International (KEI) asks that HHS take title to the four patents. The legal basis for the proposed remedy is set out in the attached memorandum, *Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions*.¹ One of the possible remedies for non-disclosures, as set out in 35 U.S.C. § 202(c)(1) and 37 C.F.R. § 401.14, is for the federal government to take possession of the patent title.

We believe this is an egregious case of non-disclosure. The same three inventors are listed for each of the four patents. Collectively they were the principal investigators in NIH grants involving more than \$66 million.

- According to the NIH RePORTER database, from 1988 to 2018, William Klunk was the principal investigator for grants obtained from the NIH consisting of 52 projects, 35 sub-projects and a total funding amount of \$47,209,483.

¹ Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions. KEI Briefing Note: 2018:1. Andrew Goldman. Revised March 16, 2018.

- From 1986 to 2018, Chester A. Mathis, Jr. received NIH grants consisting of 31 projects and 12 subprojects with a total funding amount of \$14,936,292.
- From 2003 to 2013, Yanming Wang was listed as the principal investigator for 19 NIH projects involving \$4,116,038 of funding.

This actually understates the amount of federal funding involved, since the inventors have also received NIH research contracts and funding from the Department of Energy for this research.

The inventors have made references to NIH and DOE funding of their work in papers describing the inventions, but did not report the grants on the patents, and the patents do not appear in the NIH RePORTER database.

The patents were subsequently licensed to GE Healthcare. We believe the public interest would be served if the patents were licensed on a non-exclusive basis, permitting more competition in the use of the inventions, resulting in greater innovation and lower prices. Lower prices for flutemetamol F 18 may expand access to the test, which, as Medicare describes, “may be clinically useful in the work up and management of patients with cognitive impairment who are being evaluated for possible Alzheimer’s disease or other causes of cognitive decline.”²

Finally, we note that this one of several letters we have sent to the HHS and/or the NIH, regarding failure of NIH grant recipients to disclose federal funding. We are still waiting to hear the conclusions of investigations regarding Cold Spring Harbor patents on nusinersen (trade name Spinraza), the Pharmasset/Gilead patent on sofosbuvir, the Dana Farber Cancer Institute patents on midostaurin (Trade name Rydapt), multiple institutions’ (including an NIH-funded project at a foreign university) patents on Exondys 51, and the University of Pennsylvania patents on Lomitapide (trade name Juxtapid). We are making these inquiries as a public service, to ensure the public has the opportunity to benefit from the safeguards and public interest provisions in the Bayh-Dole Act, including the obligation by patent holders to make the inventions available to the public on reasonable terms, the ability of the NIH to ensure broad use of inventions for research purposes, and the requirements in the Bayh-Dole Act for domestic manufacturing of products, among other requirements.

Sincerely,



James Love, Director, KEI
james.love@keionline.org
+1.202.332.2670

² <https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/Amyloid-PET.html>

Attachments

1. Vizamyl (INN flutemetamol F 18): Failures to disclose NIH funding for four patents in the FDA Orange Book invented by William Klunk, Chester Mathis, Jr., and Yanming Wang, and assigned to the University of Pittsburgh. Knowledge Ecology International, May 18, 2018.
2. KEI-Briefing-Note-2018-1

Cc:

Dr. Francis Collins, Director, the National Institutes of Health: Francis.Collins@nih.hhs.gov

The Honorable Daniel R. Levinson, Inspector General, Office of Inspector General (OIG), HHS, Dan.Levinson@oig.hhs.gov

Ann M. Hammersla, J.D., Director, Division of Extramural Inventions and Technology Resources Office of Policy for Extramural Research Administration, hammerslaa@od.nih.gov

Rep. Tom Cole, Oklahoma, Chairman, Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, House of Representatives.

Rep. Rosa DeLauro, Connecticut, Ranking Member, Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, Committee on Appropriations, House of Representatives.

Roy Blunt, Chair, Labor, Health and Human Services, Education and Related Agencies, Committee on Appropriations, U.S. Senate

Patty Murray, Ranking Member, Labor, Health and Human Services, Education and Related Agencies, Committee on Appropriations, U.S. Senate

Vizamyl (INN Flutemetamol F 18)

Failures to disclose NIH funding for four patents in the FDA Orange Book invented by William Klunk, Chester Mathis, Jr., and Yanming Wang, and assigned to the University of Pittsburgh

Knowledge Ecology International
May 18, 2018

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Introduction

Knowledge Ecology International (KEI) asks the National Institutes of Health (NIH) to investigate whether there has been a failure to disclose NIH research funding on four patents granted that list William E. Klunk, Chester A. Mathis, Jr., and Yanming Wang as inventors. All four patents are assigned to the University of Pittsburgh.

The patents are listed as the first four patents (out of five patents) in the FDA Orange Book for the drug Vizamyl (INN flutemetamol, marketed by GE Healthcare), a nuclear imaging agent for the visualization of β -amyloid neuritic plaque density in patients being evaluated for cognitive disorders such as Alzheimer's disease.

Each of the three inventors received numerous research grants and contracts from the NIH and other federal agencies.

According to the NIH RePORTER database, from 1988 to 2018, William Klunk was the principal investigator for grants obtained from the National Institute of Health, consisting of 52 projects, 35 sub-projects and a total funding amount of \$47,209,483.

From 1986 to 2018, Chester A. Mathis, Jr. received NIH grants consisting of 31 projects and 12 subprojects with a total funding amount of \$14,936,292.

From 2003 to 2013, Yanming Wang was listed as the principal investigator for 19 NIH projects involving \$4,116,038 of funding.

Many of the NIH grants are directly related to the four patented inventions. In addition to the grants disclosed in the NIH RePORTER database, the inventors have disclosed additional research contracts or grants related to the invention from the NIH and the U.S. Department of Energy, in various academic papers describing the inventions.

The inventions are important. William Klunk and Chester Mathis received a \$100,000 Potamkin Prize award in 2008 for their research on Alzheimer's disease. Specifically, the prize was awarded for the invention and development of Pittsburgh Compound B (PiB), a radioactive amyloid plaque imaging compound that enables visualization of the β -amyloid plaque deposits (which disrupt the function of brain cells) and distinguishes between the diagnosis of Alzheimer's disease and other types of dementia.¹

Vizamyl is available in 10 or 30 mL multi-dose glass vials at a strength of 150 MBq/mL (4.05 mCi/mL), the price of 1 vial (5 mCi) is approximately \$28,000. Medicare restricts reimbursements for the tests.²

KEI is asking the NIH to take title to the patents, which is an available remedy under the Bayh-Dole Act for non-disclosure of federal funding of patented inventions. At a minimum, the Department of Health and Human Services should require the University of Pittsburgh to correct the failure to disclose the NIH grants.

What Does Vizamyl Do?

GE Healthcare³ provides the following information on Vizamyl:

Vizamyl is an imaging drug (also called a tracer) that is injected into a person's bloodstream before a positron-emission tomography (PET) scan is performed. Currently, Vizamyl is the first-and-only imaging drug approved to provide color PET images that help your doctor estimate the amount of a protein called beta amyloid in the brain.

Although most people will develop some beta amyloid in the brain during aging, those with Alzheimer's disease tend to develop more than those who do not have the disease.

...A short time after Vizamyl is injected into the bloodstream, it will attach to beta amyloid in the brain. An imaging device called a PET scanner will then take color images of the brain. A radiologist can use these images to estimate how much beta amyloid there is.

¹ [Klunk and Mathis Win Prestigious Potamkin Prize For Alzheimer's Research. 2008](#)

² Final Decision Memorandum for: CAG-00431N Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease, September 27, 2013.

<https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=265>

³ [About Vizamyl. 2017](#)

In 2010, the Centers for Disease Control reported an estimate of 5.4 million Americans affected by Alzheimer's, ranking the illness the "sixth leading cause of death among all adults and the fifth leading cause of death for those aged 65 or older".⁴

The Orange Book Patents for Vizamyl

The May 10, 2018 version of the FDA Orange Book lists five patents for Vizamyl. Four patents were assigned to the University of Pittsburgh and one was assigned to GE Healthcare Limited, in Buckinghamshire, Great Britain.

Table 1: The Orange Book Patents for Vizamyl

Patent Number	Grant	Expiration	Inventors	Assignee
7270800	9/18/2007	09/03/2025	Klunk; William E. (Pittsburgh, PA), Mathis, Jr.; Chester A. (Pittsburgh, PA), Wang; Yanming (Imperial, PA)	University of Pittsburgh
7351401	4/1/2008	01/24/2023	Klunk; William E. (Pittsburgh, PA), Mathis, Jr.; Chester A. (Pittsburgh, PA), Wang; Yanming (Imperial, PA)	University of Pittsburgh
8236282	8/8/2012	05/21/2024	Klunk; William E. (Pittsburgh, PA), Mathis, Jr.; Chester A. (Pittsburgh, PA), Wang; Yanming (Imperial, PA)	University of Pittsburgh
8691185	4/8/2014	01/24/2023	Klunk; William E. (Pittsburgh, PA), Mathis, Jr.; Chester A. (Pittsburgh, PA), Wang; Yanming (Imperial, PA)	University of Pittsburgh
8916131	12/23/2014	09/16/2028	Roed; Line (Oslo, NO), Peterson; Sarah Elizabeth (Amersham, GB)	GE Healthcare Limited (Buckinghamshire, GB)

The Klunk, Mathis, and Wang Patents that Failed to Disclose Federal Funding

The four University of Pittsburgh patents failed to disclose federal funding in the invention. The priority, file and grant dates, title, and abstract for the patents are listed in Table 2.

Table 2: The Four Amyloid Klunk, Mathis and Wang Patents

Patent Number	Priority Date	File Date	Grant Date	Title	Abstract
7270800	8/24/2000	3/14/2003	9/18/2007	Thioflavin derivatives for use in antemortem diagnosis of	This invention relates to novel thioflavin derivatives, methods of using the derivatives in, for example, in vivo imaging of patients having neuritic plaques, pharmaceutical compositions comprising the thioflavin

⁴ [Promoting Health and Independence for an Aging Population At A Glance 2017](#), September 12, 2017

				Alzheimer's disease and in vivo imaging and prevention of amyloid deposition	derivatives and method of synthesizing the compounds. The compounds find particular use in the diagnosis and treatment of patients having diseases where accumulation of neuritic plaques are prevalent. The disease states or maladies include but are not limited to Alzheimer's disease, familial Alzheimer's disease, Down's Syndrome and homozygotes for the apolipoprotein E4 allele.
7351401	8/24/2000	6/3/2004	4/01/2008	Thioflavin derivatives for use in the antemortem diagnosis of Alzheimers disease and in vivo imaging and prevention of amyloid deposition	This invention relates to novel thioflavin derivatives, methods of using the derivatives in, for example, in vivo imaging of patients having neuritic plaques, pharmaceutical compositions comprising the thioflavin derivatives and method of synthesizing the compounds. The compounds find particular use in the diagnosis and treatment of patients having diseases where accumulation of neuritic plaques are prevalent. The disease states or maladies include but are not limited to Alzheimer's Disease, familial Alzheimer's Disease, Down's Syndrome and homozygotes for the apolipoprotein E4 allele.
8236282	8/22/2003	9/30/2009	8/7/2012	Benzothiazole derivative compounds, compositions and uses	This invention provides benzothiazole derivative compounds, compositions comprising such compounds, methods of preparing such compounds, and methods of using such compounds for detecting amyloid deposit(s) and for diagnosing a disease, disorder or condition characterized by amyloid deposit(s).
8691185	08/22/2003	7/12/2012	4/8/2014	Benzothiazole derivative compounds, compositions and uses	This invention provides benzothiazole derivative compounds, compositions comprising such compounds, methods of preparing such compounds, and methods of using such compounds for detecting amyloid deposit(s) and for diagnosing a disease, disorder or condition characterized by amyloid deposit(s).

Note that all four patents have the same three inventors (Klunk, Mathis and Wang). The first two patents have the same title, abstract and priority date. The last two patents have the same title, abstract and priority date.

The 7,270,800 and 7,351,401 patents

The 7,270,800 and 7,351,401 patents have the same three inventors (Klunk, Mathis and Wang), title and abstract, with somewhat different claims. The inventions involve novel thioflavin derivatives, and their use in in vivo imaging, for diagnosis and treatment of patients having diseases where accumulation of neuritic plaques are prevalent, including but not limited to Alzheimer's disease. The priority date for both patents is August 24, 2000, and the filing dates were May 14, 2003 and June 3, 2004.

Table 3 lists eight NIH-funded projects by the University of Pittsburgh from 1988 to 1999 that list William Klunk as the Principal Investigator. This is the time leading up to the priority date for patents 7,270,800 and 7,351,401.

Table 3: NIH-Funded Projects to the University of Pittsburgh from Fiscal Years 1988 to 1999 Listing William Klunk as PI

Project Number	Title	FY	Agency	Amount
1 F32 AG005443 01	<u>MOLECULAR PROBES FOR ALZHEIMER BETA-AMYLOID PROTEIN</u>	1988	NIA	\$27,000
5 F32 AG005443 02	<u>MOLECULAR PROBES FOR ALZHEIMER BETA-AMYLOID PROTEIN</u>	1989	NIA	\$31,750
5 R01 AG005657 06	<u>NMR STUDIES OF BRAIN AGING IN ALZHEIMER'S DISEASE</u>	1990	NIA	\$139,105
1 R29 MH053310 01A1	<u>CLINICAL METABOLIC CORRELATION IN DEMENTIA BY PROTON NMR</u>	1995	NIMH	\$98,405
5 R29 MH053310 02	<u>CLINICAL METABOLIC CORRELATION IN DEMENTIA BY PROTON NMR</u>	1996	NIMH	\$101,910
5 R29 MH053310 03	<u>CLINICAL METABOLIC CORRELATION IN DEMENTIA BY PROTON NMR</u>	1997	NIMH	\$105,204
5 R29 MH053310 04	<u>CLINICAL METABOLIC CORRELATION IN DEMENTIA BY PROTON NMR</u>	1998	NIMH	\$108,621
5 R29 MH053310 05	<u>CLINICAL METABOLIC CORRELATION IN DEMENTIA BY PROTON NMR</u>	1999	NIMH	\$112,536

The budget end date for project 5R29MH053310-05 was June 30, 2000, less than two months before the priority date of the two patents. The abstract for that grant reads as follows:

Project Number: 5R29MH053310-05
Contact PI / Project Leader: Klunk, William E
Title: Clinical Metabolic Correlation In Dementia By Proton NMR
Awardee Organization: University Of Pittsburgh At Pittsburgh

Abstract Text:

This study proposes to perform a clinical-metabolic-neuropathological correlation in **dementia**, in particular, primary degenerative **dementia** of the **Alzheimer** type (AD). We will use clinical data on behavior, mood, function, and cognition obtained in the year preceding death as markers of severity. Proton nuclear **magnetic resonance spectroscopy** (1/H **MRS**) will be used to analyze 6 brain areas obtained at autopsy from 75 **Alzheimer's disease** (AD), 25 controls, and 15 non-AD demented controls over 5 years. The first goal is to broaden the metabolic understanding of AD and to delineate clinical-metabolic-neuropathological correlations in a way that may provide insights into the timing of pathogenetic events over the course of this dementing illness. The second goal is to provide a detailed in vitro database for future extensions of this study into 1/H **MRS** studies of living patients with AD. No such detailed database currently exists. The metabolites measurable by 1/H **MRS** include N-acetyl-L-aspartate (NAA), L-glutamate, GABA, glutamine, myo-inositol, choline- containing compounds, creatine and others. NAA is important because it is a putative neuronal marker easily detected by **in vitro** and **in vivo** 1/H **MRS** and can give an estimate of neuronal survival. Much like senile plaques and **neurofibrillary tangles**, NAA can be considered a new candidate marker of the neuropathological severity of **dementia**. The excitatory and inhibitory

amino acids also play key roles in excitotoxic theories of several **dementias**. The choline-containing compounds include a phosphodiester which is a product of membrane degradation. In addition to determining differences between AD and control, demented non-AD brains will be examined to determine the **specificity** of the changes for AD. Clinical-metabolic and metabolic-neuropathologic correlations to NAA, **senile plaques**, and **neurofibrillary tangles** will be done in an attempt to determine which changes represent early, potentially causative, events and which changes are more likely secondary effects of neurodegeneration. In addition, a separately funded study will be analyzing the tissue by 31/P **MRS** and the levels of the membrane metabolites, phosphomonoesters and phosphodiesters, will be available for correlative studies as well. We hypothesize that markers of membrane proliferation and neuronal inhibition will be elevated early in the disease and decreased at later stages. In contrast, markers of membrane degeneration and excitotoxicity will be elevated at later stages. Preliminary results suggest that the **in vitro** 1/H **MRS** studies proposed in this application could provide information that is valuable in both a diagnostic and pathophysiologic sense and be readily extended to non-invasive, longitudinal studies of living patients which could aid in monitoring the course of the illness and tracking efficacy of experimental therapies.

The 8,236,282 and 8,691,185 patents

The 8,236,282 and 8,691,185 patents have the same three inventors (Klunk, Mathis and Wang), title and abstract, with somewhat different claims. The inventions involve compositions and methods of preparing benzothiazole derivatives, for the detection and diagnosis of diseases characterized by amyloid deposits. The priority date for both patents is August 22, 2003. The filing dates were September 30, 2009 and July 12, 2012.

Table 4 lists four NIH-funded projects by the University of Pittsburgh from 2001 to 2002 that list William Klunk as the Principal Investigator.

Table 4: NIH-Funded Projects to the University of Pittsburgh from Fiscal Years 2001 to 2002 Listing William Klunk as PI

Project Number	Title	FY	Agency	Amount
1K02AG001039 01A1	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2001	NIA	\$97,686
1R01AG020226 01	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2001	NIA	\$366,936
5K02AG001039 02	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2002	NIA	\$97,686
5R01AG020226 02	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2002	NIA	\$353,050

The budget end date for project 5R01AG020226-02 was July 31, 2003, less than two months before the priority date for the 8,236,282 and 8,691,185 patents, and right before the filing of the 7,270,800 and 7,351,401 patents.

The abstract for that grant reads as follows:

Project Number: 5R01AG020226-02
Contact PI / Project Leader: Klunk, William E
Title: PET Tracers To Monitor Vaccine And Immune Therapy For AD
Awardee Organization: University Of Pittsburgh At Pittsburgh

Abstract Text:

DESCRIPTION (provided by the applicant): The deposition of beta-sheet fibrils in **Alzheimer's disease (AD)** brain has been hypothesized to be the primary cause of this devastating neurodegenerative disease. These deposits include the **amyloid-beta** (Abeta) protein in **plaques** and vascular amyloid and hyper-phosphorylated tau protein in neurofibrillary tangles, dystrophic neurites and neuropil threads. Despite the presence of this characteristic neuropathology and its critical importance in the pathophysiology of the disease, no non-invasive technique has been validated to assess the presence of these deposits in living patients. The absence of such a technique hinders early and presymptomatic diagnosis and will severely hinder the development of immune therapies aimed at prevention or reversal of beta-sheet fibril deposition. Over the past decade, our laboratory has worked to develop an in vivo **beta-sheet amyloid** fibril imaging agent. This work has resulted in a promising lead agent, [N-methyl-¹¹C]2-(4'-methylaminophenyl)-**benzothiazole** (or [11C]BTA-1) which: 1) readily enters and clears from normal rodent and baboon brain; 2) binds to synthetic Abeta with nanomolar affinity; 3) specifically stains **plaques** and **tangles** in post-mortem AD brain; 4) binds to homogenates of post-mortem AD brain frontal cortex at >10-fold higher levels than aged control brain and non-AD demented brain samples, but shows no increased **binding** in AD **cerebellum**; and 5) shows no evidence of acute toxicity in preliminary studies. Furthermore, preliminary in vivo studies using APP transgenic mice and low resolution **PET scanning** show increased accumulation in the transgenic mice. In this study, we propose to validate the use of [11C]BTA-1 for in vivo **amyloid imaging** in PS/APP transgenic mice using a small animal microPET scanner. We will correlate in vivo results with: 1) quantitative immunohistochemical and histochemical measures of amyloid deposition; 2) Abeta ELISA; and 3) ex-vivo [11C]BTA-1 levels and post-mortem [3H]BTA-1 binding. We will show feasibility of longitudinal studies of the [11C]BTA-1/microPET technique in PS/APP mice and apply the technique to study an immune therapy protocol in these mice. Our goal is to provide a tool for use by investigators developing improved immune therapy protocols in transgenic mice, thus speeding progress in this area. However, because all of the techniques developed in this proposal apply directly to human studies, completion of this study will greatly speed the development of this technology for use in human studies of anti-amyloid therapies (immune therapy and secretase inhibitor therapies).

Description of the 7,270,800; 7,351,401; 8,236,282 and 8,691,185 patents

Thioflavin T is a benzothiazole compound, a fluorescent marker or a dye, that is used for the visualization and quantification of amyloid (misfolded protein aggregates found in the brains of patients diagnosed with Alzheimer's disease). Amyloids are made up of beta sheet fibrils or structures. The binding of Thioflavin T compounds to the amyloids' beta sheets displays a major increase in fluorescence intensity, allowing quantification of amyloids and diagnosis.⁵

In 2008, two of the patents' inventors, Klunk and Mathis, published a paper in the *Journal of Alzheimer Disease and Associated Disorders*, titled "Whatever happened to Pittsburgh Compound-A?"⁶ The paper provides an overview of research undertaken in order to obtain the

⁵ (2010). Biancalana M; Koide S. "Molecular mechanism of Thioflavin-T binding to amyloid fibrils" *Biochim Biophys Acta*. 1804(7):1405-12.

⁶ (2008). Klunk WE; Mathis CA. "Whatever happened to Pittsburgh Compound-A?" *Alzheimer Dis Assoc Disord*. 22(3):198-203.

desired and most effective thioflavin derivative for the diagnosis of Alzheimer's disease. The following statements were provided:

“ . . . Pittsburgh Compound-A (PiA) represents one of the early thioflavin-T derivatives made in our amyloid-imaging tracer development program at the University of Pittsburgh.

. . . For more than a decade, we struggled with manipulating the Congo red pharmacophore into a suitable positron emission tomography (PET) amyloid tracer with only limited success. This was primarily a result of the poor brain entry of this class of compounds.

. . . The transition away from the Congo red derivatives such as the X-series began in November 1999. From that time through our present work with fluorine-18-labeled PiB derivatives, we have synthesized and tested over 350 thioflavin-T derivatives.

. . . BTA-1 (PiA) was the seventh of the thioflavin-T derivatives and was first tested with in vitro binding studies and ex vivo mouse brain entry studies in April 2000, just 5 months into our thioflavin-T exploration program.

. . . It is worth noting that we began the approval process for human studies simultaneously in Sweden and in the United States in 2001, understanding that it would take longer to begin our studies in Pittsburgh than it would to begin the Uppsala arm of this study. That process included toxicologic evaluation of the lead compound funded by a special National Institute on Aging (NIA) mechanism (NIA contract, N01- AG-9-2117).

. . . NIA had already approved funding for toxicologic evaluation of Pittsburgh Compound-A, when the suggestion came up at our weekly chemistry meeting something to the effect of, “I’ve been looking at the data and thinking, and I don’t think BTA-1 is the best compound. I think we should go with 6-OH-BTA-1 [the original name for PiB], because it is cleared from normal brain much better.” It should not be surprising that this suggestion was initially met with a degree of inertia on both sides of the Atlantic.

. . . PiB was the 23rd compound synthesized and tested in our thioflavin-T program in July 2000, so it had been on the (lab)books for more than a year before the first human study. The affinities of Pittsburgh Compound-A and PiB were never convincingly different in binding studies using A β fibrils or AD brain homogenates, but the more rapid clearance of PiB from normal animal brain was evident very early on.

. . . The case was made as follows: when compared with several other proven dopamine and serotonin neuroreceptor radiotracers on “level ground,” PiB fit the profile of a good tracer and Pittsburgh Compound-A did not.”

The research paper further discloses how the correct thioflavin derivatives (PiA and PiB) were derived for the diagnosis of Alzheimer's disease, and notes some of the relevant time periods.

The following statements were made regarding funding:

"Funding support for portions of the development program was provided by grants from The National Institutes of Health (R01 AG018402, P50 AG005133, K02 AG001039, R01 AG020226, R01 MH070729, K01 MH001976, R37 AG025516, P01 AG025204), the Alzheimer's Association (TLL-01-3381), GE Healthcare and the US Department of Energy (DE-FD02-03 ER63590)."

With the exception of grants R01 MH070729 and K01 MH001976 (PI Julie Price), all the other grants listed identified either William Klunk or Chester Mathis as the Principal Investigators.

Grant R01 AG018402

Using the NIH RePORTER database, we searched for the grant R01 AG018402. There were eight projects funded under grant R01 AG018402, where Chester Mathis was the Principal Investigator, from 2001 to 2010. The organization receiving the funding was the University of Pittsburgh.

Table 5: The Eight R01 AG018402 Projects Listing Chester Mathis as the PI and the University of Pittsburgh as the Institution

Project	Project Title	FY	Total Cost
1R01AG018402-01A1	<u>AMYLOID IMAGING AGENTS FOR POSITRON EMISSION TOMOGRAPHY</u>	2001	\$350,525
5R01AG018402-02	<u>AMYLOID IMAGING AGENTS FOR POSITRON EMISSION TOMOGRAPHY</u>	2002	\$349,224
5R01AG018402-03	<u>AMYLOID IMAGING AGENTS FOR POSITRON EMISSION TOMOGRAPHY</u>	2003	\$347,922
5R01AG018402-04	<u>AMYLOID IMAGING AGENTS FOR POSITRON EMISSION TOMOGRAPHY</u>	2004	\$346,619
2R01AG018402-05	<u>AMYLOID IMAGING AGENTS FOR POSITION EMISSION TOMOGRAPHY</u>	2007	\$339,851
5R01AG018402-06	<u>AMYLOID IMAGING AGENTS FOR POSITION EMISSION TOMOGRAPHY</u>	2008	\$376,408
5R01AG018402-07	<u>AMYLOID IMAGING AGENTS FOR POSITION EMISSION TOMOGRAPHY</u>	2009	\$394,437

5R01AG018402-08	<u>AMYLOID IMAGING AGENTS FOR POSITION EMISSION TOMOGRAPHY</u>	2010	\$357,159
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Grant P50 AG005133

Using the NIH RePORTER database, we searched for the grant P50 AG005133. There were ten sub-projects funded under grant P50 AG005133, where William Klunk was the Principal Investigator, from 2005 to 2014. The organization receiving the funding was the University of Pittsburgh.

Table 6: The Ten P50 AG005133 Projects Listing William Klunk as the PI and the University of Pittsburgh as the Institution

Project	Project Title	FY	Total Cost
2P50AG005133-22	<u>NATURAL HISTORY OF AMYLOID DEPOSITION IN FAMILIAL AD</u>	2005	\$185,625
5P50AG005133-23	<u>NATURAL HISTORY OF AMYLOID DEPOSITION IN FAMILIAL AD</u>	2006	\$128,746
5P50AG005133-24	<u>NATURAL HISTORY OF AMYLOID DEPOSITION IN FAMILIAL ALZHEIMERS DISEASE</u>	2007	\$214,077
5P50AG005133-25	<u>NATURAL HISTORY OF AMYLOID DEPOSITION IN FAMILIAL ALZHEIMERS DISEASE</u>	2008	\$215,088
5P50AG005133-26	<u>NATURAL HISTORY OF AMYLOID DEPOSITION IN FAMILIAL ALZHEIMERS DISEASE</u>	2009	\$221,371
2P50AG005133-27	<u>NATURAL HISTORY OF AMYLOID DEPOSITION FAMILIAL AD</u>	2010	\$171,025
5P50AG005133-28	<u>NATURAL HISTORY OF AMYLOID DEPOSITION FAMILIAL AD</u>	2011	\$199,286
5P50AG005133-29	<u>NATURAL HISTORY OF AMYLOID DEPOSITION FAMILIAL AD</u>	2012	\$182,113
5P50AG005133-30	<u>NATURAL HISTORY OF AMYLOID DEPOSITION FAMILIAL AD</u>	2013	\$170,365
5P50AG005133-31	<u>NATURAL HISTORY OF AMYLOID DEPOSITION FAMILIAL AD</u>	2014	\$182,280

Grant K02 AG001039

Using the NIH RePORTER database, we searched for the grant K02 AG001039. There were five projects funded under grant K02 AG001039, where William Klunk was the Principal Investigator, from 2001 to 2005. The organization receiving the funding was the University of Pittsburgh.

Table 7: The Five K02 AG001039 Projects Listing William Klunk as the PI and the University of Pittsburgh as the Institution

Project	Project Title	FY	Total Cost
1K02AG001039-01A1	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2001	\$97,686
5K02AG001039-02	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2002	\$97,686
5K02AG001039-03	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2003	\$97,686
5K02AG001039-04	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2004	\$97,686
5K02AG001039-05	<u>PET IMAGING PROBES FOR AMYLOID IN ALZHEIMERS AND AGING</u>	2005	\$97,686

Grant R01 AG020226

Using the NIH RePORTER database, we searched for the grant R01 AG020226. There were five projects funded under grant R01 AG020226, where William Klunk was the Principal Investigator, from 2001 to 2005. The organization receiving the funding was the University of Pittsburgh.

Table 8: The Five R01 AG020226 Projects Listing William Klunk as the PI and the University of Pittsburgh as the Institution

Project	Project Title	FY	Total Cost
1R01AG020226-01	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2001	\$366,936

5R01AG020226-02	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2002	\$353,050
5R01AG020226-03	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2003	\$353,050
5R01AG020226-04	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2004	\$353,050
5R01AG020226-05	<u>PET TRACERS TO MONITOR VACCINE AND IMMUNE THERAPY FOR AD</u>	2005	\$353,050

Grant R37 AG025516

Using the NIH RePORTER database, we searched for the grant R37 AG025516. There were eleven projects funded under grant R37 AG025516, where William Klunk was the Principal Investigator, from 2005 to 2014. The organization receiving the funding was the University of Pittsburgh.

Table 9: The Eleven R37 AG025516 Projects Listing William Klunk as the PI and the University of Pittsburgh as the Institution

Project	Project Title	FY	Total Cost
1R37AG025516-01	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2005	\$430,155
5R37AG025516-02	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2006	\$459,594
5R37AG025516-03	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2007	\$459,409
5R37AG025516-04	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2008	\$449,361
3R37AG025516-05S1	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2009	\$5,000

5R37AG025516-05	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2009	\$362,933
4R37AG025516-06	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2010	\$473,345
5R37AG025516-07	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2011	\$481,954
5R37AG025516-08	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2012	\$480,423
5R37AG025516-09	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2013	\$441,934
5R37AG025516-10	<u>AMYLOID PATHOLOGY AND COGNITION IN NORMAL ELDERLY</u>	2014	\$227,443

Grant P01 AG025204

Using the NIH RePORTER database, we searched for the grant P01 AG025204. There were 36 projects funded under grant P01 AG025204, where William Klunk was the Principal Investigator, from 2005 to 2018. The organization receiving the funding was the University of Pittsburgh.

Of interest are the nineteen grants listed from years 2005-2012, prior to the filing dates for two of the patents.

Table 10: The Nineteen P01 AG025204 Projects Listing William Klunk as the PI and the University of Pittsburgh as the Institution

Project	Project Title	FY	Total Cost
1P01AG025204-01	<u>CROSS-SECTIONAL ASSESSMENT OF IN VIVO AMYLOID IN MCI AND AD</u>	2005	\$157,425
5P01AG025204-02	<u>CROSS-SECTIONAL ASSESSMENT OF IN VIVO AMYLOID IN MCI AND AD</u>	2006	\$172,602
5P01AG025204-03	<u>CROSS-SECTIONAL ASSESSMENT OF IN VIVO AMYLOID IN MCI AND AD</u>	2007	\$298,271
3P01AG025204-04S1	<u>IN VIVO PIB PET AMYLOID IMAGING: NORMALS, MCI & DEMENTIA</u>	2008	\$142,645

KEI Series on inventors that fail to disclose U.S. government funding in patented inventions

5P01AG025204-04	<u>CROSS-SECTIONAL ASSESSMENT OF IN VIVO AMYLOID IN MCI AND AD</u>	2008	\$259,127
5P01AG025204-04	<u>IN VIVO PIB PET AMYLOID IMAGING: NORMALS, MCI & DEMENTIA</u>	2008	\$1,031,916
5P01AG025204-05	<u>CROSS-SECTIONAL ASSESSMENT OF IN VIVO AMYLOID IN MCI AND AD</u>	2009	\$360,047
5P01AG025204-05	<u>IN VIVO PIB PET AMYLOID IMAGING: NORMALS, MCI & DEMENTIA</u>	2009	\$1,151,713
2P01AG025204-06	<u>ADMINISTRATIVE CORE</u>	2010	\$129,363
2P01AG025204-06	<u>MODULATORS OF COGNITIVE TRANSITION FROM MCI TO AD</u>	2010	\$301,836
2P01AG025204-06	<u>IN VIVO PIB PET AMYLOID IMAGING: NORMALS, MCI & DEMENTIA</u>	2010	\$1,538,583
5P01AG025204-07	<u>ADMINISTRATIVE CORE</u>	2011	\$126,512
5P01AG025204-07	<u>MODULATORS OF COGNITIVE TRANSITION FROM MCI TO AD</u>	2011	\$346,486
5P01AG025204-07	<u>QUANTITATIVE NEUROPATHOLOGICAL CORRELATES OF IN VIVO PIB RETENTION</u>	2011	\$292,634
5P01AG025204-07	<u>IN VIVO PIB PET AMYLOID IMAGING: NORMALS, MCI & DEMENTIA</u>	2011	\$1,482,584
5P01AG025204-08	<u>ADMINISTRATIVE CORE</u>	2012	\$126,424
5P01AG025204-08	<u>MODULATORS OF COGNITIVE TRANSITION FROM MCI TO AD</u>	2012	\$337,923
5P01AG025204-08	<u>QUANTITATIVE NEUROPATHOLOGICAL CORRELATES OF IN VIVO PIB RETENTION</u>	2012	\$287,620
5P01AG025204-08	<u>IN VIVO PIB PET AMYLOID IMAGING: NORMALS, MCI & DEMENTIA</u>	2012	\$1,420,069

Additional Notes on Research Grants from the National Institutes of Health

NIH Grants to William Klunk Cited in a 2003 Paper

In 2003, the patents' inventors, Klunk, Mathis and Wang, published a paper in the journal *Proceedings of the National Academy of Sciences of the United States of America* along with seven co-authors, titled "Four-dimensional multiphoton imaging of brain entry, amyloid binding, and clearance of an amyloid-beta ligand in transgenic mice."⁷ The paper made disclosures regarding funding, including NIH grants to Mathis and Klunk:

"...This work supported by National Institutes of Health Grants AG08487 (to B.T.H.), AG18402 (to C.A.M.), AG01039 (to W.E.K.), AG20226 (to W.E.K.), AG15453 (to B.T.H.), EB00768 (to B.J.B.), and AG020570 (to B.J.B.), an Alzheimer Association Pioneer Award (to B.T.H.), Alzheimer Association Grants IIRG-95-076 (to W.E.K.), TLL-01-3381 (to W.E.K.), and NIRG-00-2355 (to Y.W.), and Institute for the Study of Aging/American Federation for Aging Research Grant 210304 (to Y.W.)."

The abstract for Bacskai *et al.* 2003 reads as follows:

"The lack of a specific biomarker makes preclinical diagnosis of **Alzheimer's disease** (AD) impossible, and it precludes assessment of therapies aimed at preventing or reversing the course of the disease. The development of a tool that enables direct, quantitative detection of the **amyloid-beta deposits** found in the disease would provide an excellent biomarker. This article demonstrates the real-time biodistribution kinetics of an imaging agent in transgenic mouse models of **AD**. Using multiphoton microscopy, **Pittsburgh compound B (PIB)** was imaged with sub- μ m resolution in the brains of living transgenic mice during peripheral administration. **PIB** entered the brain quickly and labeled **amyloid deposits** within minutes. The nonspecific **binding** was cleared rapidly, whereas specific labeling was prolonged. WT mice showed rapid brain entry and clearance of **PIB** without any binding. These results demonstrate that the compound **PIB** has the properties required for a good amyloid-imaging agent in humans with or at risk for **AD**."

NIH Grants to Chester Mathis Cited in a 2004 Paper

In 2004, the patents inventors, Klunk, Mathis and Wang, published a paper in the journal *Annals of Neurology* along with eighteen co-authors, titled "Imaging brain amyloid in Alzheimer's

⁷ (2003). Bacskai BJ; Hickey GA; Skoch J; Kajdasz ST; Wang Y; Huang GF; Mathis CA; Klunk WE; Hyman BT. "Four-dimensional multiphoton imaging of brain entry, amyloid binding, and clearance of an amyloid-beta ligand in transgenic mice." *Proc Natl Acad Sci U S A*. 100(21):12462-7.

disease with Pittsburgh Compound-B.”⁸ PubMed provides the following information on the grant support:

“Grant support

AG 01039/AG/NIA NIH HHS/United States

AG 05133/AG/NIA NIH HHS/United States

AG 18402/AG/NIA NIH HHS/United States

AG 20226/AG/NIA NIH HHS/United States”

The abstract for Klunk *et al.* 2004 reads as follows:

“This report describes the first human study of a novel **amyloid-imaging positron emission tomography (PET)** tracer, termed **Pittsburgh Compound-B (PIB)**, in 16 patients with diagnosed mild **AD** and 9 controls. Compared with controls, **AD** patients typically showed marked retention of **PIB** in areas of association cortex known to contain large amounts of amyloid deposits in **AD**. In the **AD** patient group, **PIB** retention was increased most prominently in frontal cortex (1.94-fold, $p = 0.0001$). Large increases also were observed in parietal (1.71-fold, $p = 0.0002$), temporal (1.52-fold, $p = 0.002$), and occipital (1.54-fold, $p = 0.002$) cortex and the striatum (1.76-fold, $p = 0.0001$). **PIB** retention was equivalent in **AD** patients and controls in areas known to be relatively unaffected by **amyloid** deposition (such as subcortical white matter, pons, and cerebellum). Studies in three young (21 years) and six older healthy controls (69.5 ± 11 years) showed low **PIB** retention in cortical areas and no significant group differences between young and older controls. In cortical areas, **PIB** retention correlated inversely with cerebral glucose metabolism determined with 18F-fluorodeoxyglucose. This relationship was most robust in the parietal cortex ($r = -0.72$; $p = 0.0001$). The results suggest that **PET** imaging with the novel tracer, **PIB**, can provide quantitative information on **amyloid deposits** in living subjects.

NIH Grants to Yanming Wang

In 2004, the patents’ inventors, Klunk, Mathis and Wang, published a paper in the *Journal of Molecular Neuroscience* along with four co-authors, titled “development of a PET/SPECT agent for amyloid imaging in Alzheimer’s disease.”⁹ PubMed provides the following information on the grant support:

⁸ (2004). Klunk WE; Engler H; Nordberg A; Wang Y; Blomqvist G; Holt DP; Bergström M; Savitcheva I; Huang GF; Estrada S; Ausén B; Debnath ML; Barletta J; Price JC; Sandell J; Lopresti BJ; Wall A; Koivisto P; Antoni G; Mathis CA; Långström B. “Imaging brain amyloid in Alzheimer’s disease with Pittsburgh Compound-B.” *Ann Neurol.* 55(3):306-19.

⁹ (2004). Wang Y; Klunk WE; Debnath ML; Huang GF; Holt DP; Shao L; Mathis CA. “Development of a PET/SPECT agent for amyloid imaging in Alzheimer’s disease.” *J Mol Neurosci.* 24(1):55-62.

“Grant support
AG01039/AG/NIA NIH HHS/United States
AG05133/AG/NIA NIH HHS/United States
AG18402/AG/NIA NIH HHS/United States
AG20226/AG/NIA NIH HHS/United States
AG22048-01A1/AG/NIA NIH HHS/United States”

The abstract for Wang *et al.* 2004 reads as follows:

“In the search for a cure for **Alzheimer's disease (AD)**, efforts have been focused on preventing or reversing **amyloid deposition** in the **brain**. Efficacy evaluation of these anti-amyloid therapies would greatly benefit from development of a tool for the **in vivo** detection and quantitation of **amyloid deposits** in the brain. Toward this goal, we have developed a series of **benzothiazole derivatives** as **amyloid-imaging agents** for **positron emission tomography (PET)**. To extend the potential of these **amyloid-imaging agents** for routine clinical studies, we also set out to develop iodinated **benzothiazole derivatives** that could be used as dual agents for either PET or the complementary **single photon emission computed tomography (SPECT)**. Such dual agents would permit **PET** or **SPECT** studies using radiotracers with the same chemical identity but labeled with different radionuclides. This would facilitate the validation of clinical **SPECT** studies, based on quantitative **PET** studies. In this work we report the synthesis and biological evaluation of a potent, selective, and brain-permeable benzothiazole compound, 2-(3'-iodo-4'-methylaminophenyl)-6-hydroxy-benzothiazole, termed 6-OH-BTA-1-3'-I (4), which can be **radiolabeled** with either positron-emitting carbon-11 or single photon-emitting iodine-125/iodine-123. The synthesis and radiolabeling of [125I]4 or [11C]4 were achieved through direct iodination with sodium [125I]iodide in the presence of chloramine T or through radiomethylation with [11C]CH₃I. **In vitro amyloid binding** assays indicated that [125I]4 bound to **amyloid deposits** in a saturable manner and exhibited affinities in the nanomolar concentration range. Binding studies of [125I]4 to postmortem human brain homogenates also showed preference of binding to frontal cortex in the **AD** homogenates relative to age-matched control **homogenates** or **cerebellum** from either **AD** or control. **In vivo** pharmacokinetic studies in normal mice following iv injection of [11C]4 indicated that the **radioligand** entered the **brain** readily at early time points and cleared from the **brain** rapidly at later time points with a 2- to 30-min ratio >3. These results suggest that the new radioiodinated **benzothiazole ligand** might be useful as a surrogate marker for the in vivo quantitation of **amyloid deposition** in human brain for use with either **PET** or **SPECT**.”

According to the NIH RePORTER database, Yanming Wang received a total of \$602,463 to support five projects that mention amyloid and involve diagnostics tests for dementia and/or Alzheimer's disease.

Table 11: Five NIH Grants to Yanming Wang from 2003-2007 Mentioning Amyloid-based Screening for Alzheimer's and Dementia

Grant Number	Title	Budget Start Date	Budget End Date	Agency
1K25AG022048-01A1	<u>QUANTITATIVE IMAGING OF AMYLOID DEPOSITS IN AD AND AGING</u>	9/30/2003	8/31/2004	NIA
7K25AG022048-02	<u>QUANTITATIVE IMAGING OF AMYLOID DEPOSITS IN AD AND AGING</u>	9/15/2004	8/31/2005	NIA
5K25AG022048-03	<u>QUANTITATIVE IMAGING OF AMYLOID DEPOSITS IN AD AND AGING</u>	9/1/2005	7/14/2006	NIA
7K25AG022048-04	<u>QUANTITATIVE IMAGING OF AMYLOID DEPOSITS IN AD AND AGING</u>	9/1/2006	8/31/2007	NIA
5K25AG022048-05	<u>QUANTITATIVE IMAGING OF AMYLOID DEPOSITS IN AD AND AGING</u>	9/1/2007	8/31/2008	NIA

Why the Wang Grants are Related to the Inventions

The abstracts given for the grants are as follows:

The Abstract for the Wang Amyloid Grants listed in Table 11

1K25AG022048-01A1, 7K25AG022048-02, 5K25AG022048-03, 7K25AG022048-04 and 5K25AG022048-05

DESCRIPTION (provided by applicant): In this application for a Mentored Quantitative Research Career Development Award (K25), the candidate's research and career development plans are described. The project is designed to customize the educational and research activities for the candidate to achieve two major goals. The immediate goal is for the candidate to continue his research in **amyloid imaging in Alzheimer's disease** and aging. The long-term goal is for the candidate to acquire advanced biomedical research skills and develop as an independent researcher in aging-related biomedical imaging. To achieve these goals, the candidate will obtain further trainings in neuroscience, biostatistics, pharmacology, and pharmacokinetics as well as in responsible conduct of biomedical and clinical research. He will also acquire related knowledge through journal clubs, research seminars, lectures, and conferences, and through interaction with other investigators and trainees. The practical skills in biomedical imaging will primarily be obtained through the proposed microPET studies under the guidance of Drs. Mathis and Klunk at the University of Pittsburgh. In this proposed research, the candidate plans to use microPET to evaluate amyloid-imaging agents in transgenic mice models of **amyloid deposition**. This will allow us for the first time to evaluate the in vivo binding specificity and pharmacokinetic profiles of lead compounds in a CNS model that mimics the future human studies. Therefore, this project will satisfy the following specific aims: 1) rationally design and synthesize a selected array of amyloid-binding agents; 2) evaluate the new compounds for in vitro binding affinity and specificity for amyloid deposits; 3) evaluate selected compounds in ex vivo studies of brain entry, clearance; and metabolism in normal control mice with no amyloid deposits in the brain; 4) use microPET to assess the in vivo properties of selected compounds in amyloid-containing transgenic mouse models to determine **in vivo**

binding specificity and detailed pharmacokinetic profiles. The overall goal of our research is to identify potent, selective, and brain permeable amyloid probes suitable for in vivo human studies.

The patents listed above in Table 2 provide several key terms/words that appear to be the subject matter of the grants listed in Table 11, including, to mention a few:

- These facts have little implications for **amyloid imaging** studies in which an extremely minute amount of the high specific activity radiolabelled dye would be directly injected into the blood stream. (PAGE 4, PATENT 7,351,401)
- The disease states or maladies include but are not limited to **Alzheimer's Disease**, familial **Alzheimer's Disease**, Down's Syndrome and homozygotes for the apolipoprotein E4 allele. (ABSTRACT, PATENT 7270800)
- **In Vivo** Baboon Imaging Studies (PAGE 17, PATENT 8,236,282)
- In allowing the temporal sequence of **amyloid deposition** to be followed, the inventive compound may further be used to correlate **amyloid deposition** with the onset of clinical symptoms associated with a disease, disorder or condition. (PAGE 5, PATENT 8,236,282)
- This study reflects **brain entry** and clearance from normal brain tissue. (PAGE 16, PATENT 8,236,282)

The Vizamyl Prices

Vizamyl injection is available in 10 or 30 mL multi-dose glass vial at a strength of 150 MBq/mL (4.05 mCi/mL). The price of 1 vial (5 mCi) is approximately \$28,000.¹⁰

Requested Remedies for Non-disclosure

The Bayh-Dole Act and federal regulations and guidelines obligate contractors to disclose government rights in subject inventions, including via: (1) a requirement to disclose within a reasonable time that federal funding contributed to a subject invention; (2) contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

After establishing a failure by the patent holder to disclose the federal funding, an agency may choose to require the patent holders to provide a disclosure to iEdison and to submit a Certificate of Correction to the United States Patent and Trademark (USPTO). The agency also has consequential remedies. In particular, a failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the federal government to "receive title to any subject invention not disclosed to it within such time."

¹⁰ <https://www.rxgo.com/drug/vizamyl-coupon>

The disclosure itself is an acknowledgement that the federal government has certain rights in the patents, and that the patent holder has certain obligations. When federal funding is involved, the patent owner has an obligation to manufacture the invention substantially within the United States and to make the invention "available to the public on reasonable terms." The federal government possesses a worldwide royalty-free right to use the patent, and may grant a compulsory license to the patent under the Bayh-Dole march-In provisions of 35 U.S.C. § 203(a).

The failure to make a timely disclosure of the federal funding should be seen as an attempt to evade these responsibilities and as a denial of the government's rights in the invention.

KEI recommends that the federal government take title to the invention, since the lesser remedy of requiring late disclosure has not, in the past, provided an adequate incentive for patent holders to comply with the disclosure obligations.

For a more detailed discussion of the specific statutory, regulatory and contractual obligations to disclose federal funding in patented inventions, and the remedies when funding is not disclosed, see: [KEI Briefing Note 2018:1](#).

ANNEX 1: Select News Reports and Other Background on Vizamyl

[About Alzheimer's disease](#). Alzheimer's Association.

2014. Scott Lerman. [GE Healthcare Announces European Union Approval of VIZAMYL™ \(Flutemetamol \(18F\) Solution for Injection\) for PET Imaging of Beta Amyloid Plaque in Suspected Alzheimer's Disease](#). *Business Wire*. September 1, 2014.

2015. Lauren Dubinsky. [GE's Vizamyl improves diagnostic confidence for early-onset dementia](#). *DOTmed*. July 22, 2015.

ANNEX 2: NIH Grants to the University of Pittsburgh with William E. Klunk Listed as Principal Investigator, with Search Term "Amyloid"

The search term for NIH RePORTER database: "Text Search: amyloid (and); Search in: Projects, AdminIC: All; Principal Investigator / Project Leader: Klunk; William; Fiscal Year: All Fiscal Years."

KEI Series on inventors that fail to disclose U.S. government funding in patented inventions

Project Number	Project Title	Fiscal Year	FY Cost
1F32AG005443-01	Molecular Probes For Alzheimer Beta-amyloid Protein	1988	\$27,000
5F32AG005443-02	Molecular Probes For Alzheimer Beta-amyloid Protein	1989	\$31,750
1K02AG001039-01A1	Pet Imaging Probes For Amyloid In Alzheimers And Aging	2001	\$97,686
1R01AG020226-01	Pet Tracers To Monitor Vaccine And Immune Therapy For AD	2001	\$366,936
5K02AG001039-02	Pet Imaging Probes For Amyloid In Alzheimers And Aging	2002	\$97,686
5R01AG020226-02	Pet Tracers To Monitor Vaccine And Immune Therapy For AD	2002	\$353,050
5K02AG001039-03	Pet Imaging Probes For Amyloid In Alzheimers And Aging	2003	\$97,686
5R01AG020226-03	Pet Tracers To Monitor Vaccine And Immune Therapy For AD	2003	\$353,050
5R01AG020226-04	Pet Tracers To Monitor Vaccine And Immune Therapy For AD	2004	\$353,050
5K02AG001039-04	Pet Imaging Probes For Amyloid In Alzheimers And Aging	2004	\$97,686
5K02AG001039-05	Pet Imaging Probes For Amyloid In Alzheimers And Aging	2005	\$97,686
1R37AG025516-01	Amyloid Pathology And Cognition In Normal Elderly	2005	\$430,155
1P01AG025204-01	Cross-sectional Assessment Of In Vivo Amyloid In Mci And AD	2005	\$157,425
2P50AG005133-22	Natural History Of Amyloid Deposition In Familial AD	2005	\$185,625
5R01AG020226-05	Pet Tracers To Monitor Vaccine And Immune Therapy For AD	2005	\$353,050
5P50AG005133-23	Natural History Of Amyloid Deposition In Familial AD	2006	\$128,746
5P01AG025204-02	Cross-sectional Assessment Of In Vivo Amyloid In Mci And AD	2006	\$172,602
1U01AG028526-01	Amyloid-lowering Small Molecule Ab-binding Agents In AD	2006	\$459,078
5R37AG025516-02	Amyloid Pathology And Cognition In Normal Elderly	2006	\$459,594
5P01AG025204-03	Cross-sectional Assessment Of In Vivo Amyloid In Mci And AD	2007	\$298,271
5U01AG028526-02	Amyloid-lowering Small Molecule Ab-binding Agents In AD	2007	\$450,738
5P50AG005133-24	Natural History Of Amyloid Deposition In Familial Alzheimers Disease	2007	\$214,077
5R37AG025516-03	Amyloid Pathology And Cognition In Normal Elderly	2007	\$459,409
5R37AG025516-04	Amyloid Pathology And Cognition In Normal Elderly	2008	\$449,361
5P50AG005133-25	Natural History Of Amyloid Deposition In Familial Alzheimers Disease	2008	\$215,088
3P01AG025204-04S1	In Vivopib Pet Amyloid Imaging: Normals; Mci & Dementia	2008	\$142,645
5P01AG025204-04	In Vivopib Pet Amyloid Imaging: Normals; Mci & Dementia	2008	\$1,031,916
5U01AG028526-03	Amyloid-lowering Small Molecule Ab-binding Agents In AD	2008	\$454,087
5P01AG025204-04	Cross-sectional Assessment Of In Vivo Amyloid In Mci And AD	2008	\$259,127

KEI Series on inventors that fail to disclose U.S. government funding in patented inventions

5P50AG005133-26	Natural History Of Amyloid Deposition In Familial Alzheimers Disease	2009	\$221,371
5P01AG025204-05	In Vivopib Pet Amyloid Imaging: Normals; Mci & Dementia	2009	\$1,151,713
5U01AG028526-04	Amyloid-lowering Small Molecule Ab-binding Agents In AD	2009	\$466,821
5R37AG025516-05	Amyloid Pathology And Cognition In Normal Elderly	2009	\$362,933
5P01AG025204-05	Cross-sectional Assessment Of In Vivo Amyloid In Mci And AD	2009	\$360,047
3R37AG025516-05S1	Amyloid Pathology And Cognition In Normal Elderly	2009	\$5,000
2P01AG025204-06	Modulators Of Cognitive Transifion From Mci To AD	2010	\$301,836
4R37AG025516-06	Amyloid Pathology And Cognition In Normal Elderly	2010	\$473,345
2P01AG025204-06	In Vivo Pib Pet Amyloid Imaging: Normals; Mci & Dementia	2010	\$1,538,583
5U01AG028526-05	Amyloid-lowering Small Molecule Ab-binding Agents In AD	2010	\$504,093
5P01AG025204-07	In Vivo Pib Pet Amyloid Imaging: Normals; Mci & Dementia	2011	\$1,482,584
5R37AG025516-07	Amyloid Pathology And Cognition In Normal Elderly	2011	\$481,954
5P50AG005133-28	Natural History Of Amyloid Deposition Familial Ad	2011	\$199,286
5P50AG005133-29	Natural History Of Amyloid Deposition Familial Ad	2012	\$182,113
5P01AG025204-08	Administrative Core	2012	\$126,424
5P01AG025204-08	Modulators Of Cognitive Transifion From Mci To Ad	2012	\$337,923
5P01AG025204-08	Quantitative Neuropathological Correlates Of In Vivo Pib Retention	2012	\$287,620
5R37AG025516-08	Amyloid Pathology And Cognition In Normal Elderly	2012	\$480,423
5P01AG025204-08	In Vivo Pib Pet Amyloid Imaging: Normals; Mci & Dementia	2012	\$1,420,069
5R37AG025516-09	Amyloid Pathology And Cognition In Normal Elderly	2013	\$441,934
5P01AG025204-09	Modulators Of Cognitive Transifion From Mci To Ad	2013	\$267,813
5P01AG025204-09	Administrative Core	2013	\$113,777
5P01AG025204-09	Quantitative Neuropathological Correlates Of In Vivo Pib Retention	2013	\$274,558
5P01AG025204-09	In Vivo Pib Pet Amyloid Imaging: Normals; Mci & Dementia	2013	\$1,295,247
5P50AG005133-30	Natural History Of Amyloid Deposition Familial Ad	2013	\$170,365
2RF1AG025516-11	Amyloid Pathology And Cognition In Normal Elderly	2014	\$2,701,818
5P01AG025204-10	Administrative Core	2014	\$126,259
5P01AG025204-10	Modulators Of Cognitive Transifion From Mci To Ad	2014	\$175,638
5P01AG025204-10	Quantitative Neuropathological Correlates Of In Vivo Pib Retention	2014	\$286,635
5P01AG025204-10	In Vivo Pib Pet Amyloid Imaging: Normals; Mci & Dementia	2014	\$1,146,355
5R37AG025516-10	Amyloid Pathology And Cognition In Normal Elderly	2014	\$227,443
5P50AG005133-31	Natural History Of Amyloid Deposition Familial Ad	2014	\$182,280

KEI Series on inventors that fail to disclose U.S. government funding in patented inventions

1U01AG051406-01	Neurodegeneration In Aging Down Syndrome (niad): A Longitudinal Study Of Cognition And Biomarkers Of Alzheimer's Disease	2015	\$3,656,559
2P01AG025204-11A1	Imaging Pathophysiology In Aging And Neurodegeneration	2016	\$1,998,101
3RF1AG025516-11S1	Amyloid Pathology And Cognition In Normal Elderly	2016	\$782,946
5U01AG051406-02	Neurodegeneration In Aging Down Syndrome (niad): A Longitudinal Study Of Cognition And Biomarkers Of Alzheimer's Disease	2016	\$3,556,865
3U01AG051406-03S1	Neurodegeneration In Aging Down Syndrome (niad): A Longitudinal Study Of Cognition And Biomarkers Of Alzheimer's Disease	2017	\$158,939
5P01AG025204-12	Imaging Pathophysiology In Aging And Neurodegeneration	2017	\$2,020,576
3U01AG051406-03S2	Neurodegeneration In Aging Down Syndrome (niad): A Longitudinal Study Of Cognition And Biomarkers Of Alzheimer's Disease	2017	\$163,334
5U01AG051406-03	Neurodegeneration In Aging Down Syndrome (niad): A Longitudinal Study Of Cognition And Biomarkers Of Alzheimer's Disease	2017	\$3,623,562

ANNEX 3: Eighteen Patents Assigned to the University of Pittsburgh that List William E. Klunk as the Inventor

Note: only one patent disclosed federal funding.

Patent Number	Title
<u>9,833,458</u>	<u>Thioflavin derivatives for use in the antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>9,808,541</u>	<u>Thioflavin derivatives for use in antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>9,134,328</u>	<u>Methods of using benzothiazole derivative compounds and compositions</u>
<u>8,911,707</u>	<u>Thioflavin derivatives for use in antemortem diagnosis of alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>8,691,185</u>	<u>Benzothiazole derivative compounds, compositions and uses</u>
<u>8,580,229</u>	<u>Amyloid imaging as a surrogate marker for efficacy of anti-amyloid therapies</u>

<u>8,404,213</u>	<u>Thioflavin derivatives for use in antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>8,343,457</u>	<u>Amyloid imaging as a surrogate marker for efficacy of anti-amyloid therapies</u>
<u>8,236,282</u>	<u>Benzothiazole derivative compounds, compositions and uses</u>
<u>8,147,798</u>	<u>Amyloid imaging as a surrogate marker for efficacy of anti-amyloid therapies</u>
<u>8,138,360</u>	<u>Isotopically-labeled benzofuran compounds as imaging agents for amyloidogenic proteins</u>
<u>7,854,920</u>	<u>Thioflavin derivatives for use in antemortem diagnosis of alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>7,351,401</u>	<u>Thioflavin derivatives for use in the antemortem diagnosis of Alzheimers disease and in vivo imaging and prevention of amyloid deposition</u>
<u>7,270,800</u>	<u>Thioflavin derivatives for use in antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>6,417,178</u>	<u>Amyloid binding nitrogen-linked compounds for the antemortem diagnosis of alzheimer's disease, in vivo imaging and prevention of amyloid deposits</u>
<u>6,168,776</u>	<u>Alkyl, alkenyl and alkynyl Chrysamine G derivatives for the antemortem diagnosis of Alzheimer's disease and in vivo imaging and prevention of amyloid deposition</u>
<u>6,133,259</u>	<u>Alkyl, alkenyl and alkynyl chrysamine G derivatives for inhibition of cell degeneration and toxicity associated with amyloid deposition</u>
<u>6,1144,175</u>	<u>Compound for the antemortem diagnosis of Alzheimer's Disease and in vivo imaging and prevention of amyloid deposition</u>

ANNEX 4: NIH Grants to the University of Pittsburgh with Chester A. Mathis Listed as Principal Investigator, with Search Term "Amyloid"

The search term for NIH RePORTER database: "Text Search: amyloid (and); Search in: Projects, AdminIC: All; Principal Investigator / Project Leader: Mathis; Chester; Fiscal Year: All Fiscal Years."

KEI Series on inventors that fail to disclose U.S. government funding in patented inventions

Project Number	Project Title	Agency	FY	FY Cost
1R01AG018402-01A1	Amyloid Imaging Agents For Positron Emission Tomography	NIA	2001	\$350,525
5R01AG018402-02	Amyloid Imaging Agents For Positron Emission Tomography	NIA	2002	\$349,224
5R01AG018402-03	Amyloid Imaging Agents For Positron Emission Tomography	NIA	2003	\$347,922
5R01AG018402-04	Amyloid Imaging Agents For Positron Emission Tomography	NIA	2004	\$346,619
2R01AG018402-05	Amyloid Imaging Agents For Position Emission Tomography	NIA	2007	\$339,851
5R01AG018402-06	Amyloid Imaging Agents For Position Emission Tomography	NIA	2008	\$376,408
5R01AG018402-07	Amyloid Imaging Agents For Position Emission Tomography	NIA	2009	\$394,437
5R01AG018402-08	Amyloid Imaging Agents For Position Emission Tomography	NIA	2010	\$357,159
1S10RR028324-01	Siemens Eclipse Hp Cyclotron For Pet Imaging Research	NCRR	2010	\$2,688,777
2P50AG005133-32	Project 2: Pet Imaging Of Tau In Elderly Controls; Mci; And Ad	NIA	2015	\$137,119
5P50AG005133-33	Project 2: Pet Imaging Of Tau In Elderly Controls; Mci; And Ad	NIA	2016	\$137,119
5P50AG005133-34	Project 2: Pet Imaging Of Tau In Elderly Controls; Mci; And Ad	NIA	2017	\$137,119

Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions

KEI Briefing Note: 2018:1. Andrew Goldman. Revised March 16, 2018

Legal, Regulatory, and Contractual Obligations¹

The Bayh-Dole Act and federal regulations and guidelines make clear several obligations for contractors in the disclosure of government rights in subject inventions, including: (1) a requirement to disclose that federal funding contributed to an invention; (2) contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

First, contractors are required to disclose subject inventions discovered with federal funding in a timely manner and with sufficient detail to describe the invention.

Under 35 U.S.C. § 202(c)(1), any contractor that receives funding from the federal government is required to “disclose each subject invention to the Federal agency within a reasonable time after it becomes known to contractor personnel responsible for the administration of patent matters.”²

Under 37 C.F.R. § 401.3(a), each federal funding agreement shall contain the “standard patent rights clause” found at 37 C.F.R. § 401.14(a), barring specific circumstances and exceptions.³ Subsection (c)(1) of the patent rights clause outlines the disclosure requirements, including a two month time limit on the disclosure of patents and a requirement that the disclosure have sufficient detail:⁴

37 C.F.R. § 401.14(a)(c)(1)

(c) Invention Disclosure, Election of Title and Filing of Patent Application by *Contractor*

(1) The *contractor* will disclose each subject invention to the *Federal Agency* within two months after the inventor discloses it in writing to *contractor* personnel responsible for patent matters. The disclosure to the *agency* shall be in the form of a written report and shall identify the contract under which the invention was made and the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or

¹ See: <https://www.keionline.org/bayh-dole/failure-to-disclose>

² The statute defines a “subject invention” at 35 U.S.C. § 201(e) as “any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement,” and defines a contractor at 35 U.S.C. § 201(c) as “any person, small business firm, or nonprofit organization that is party to a funding agreement.”

³ The exceptions do not contain reference to the disclosure requirements.

⁴ Italics in original.

electrical characteristics of the invention. The disclosure shall also identify any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure. In addition, after disclosure to the *agency*, the *Contractor* will promptly notify the *agency* of the acceptance of any manuscript describing the invention for publication or of any on sale or public use planned by the *contractor*.

...

(4) Requests for extension of the time for disclosure, election, and filing under subparagraphs (1), (2), and (3) may, at the discretion of the *agency*, be granted.

Second, in implementing this regulation, agencies may require disclosure through documentation and/or via iEdison, an online electronic system for reporting inventions and patents discovered under federal grants, or via other documents to be submitted.⁵ iEdison is run by the National Institutes of Health (NIH), but is used by a wide variety of agencies, including:

Agency for Health Care Research and Quality (AHRQ)
Agricultural Research Service (ARS)
Agency for Toxic Substances and Disease Registry (ATSDR)
Air Force Office of Scientific Research (AFOSR)
Air Force Research Laboratory Information Directorate (AFRL/RI)
Air Force Materiel Command Legal Office (AFMCLO/JAZ)
Army Medical Research and Materiel Command (ARMY/MRMC)
Army Natick Soldier Systems Center (ARMY/SSC)
Army Research Laboratory (ARMY/ARL)
Army Research Office (ARMY/ARO)
Army Space and Missile Defense Command (ARMY/SMDC)
Centers for Disease Control and Prevention (CDC)
Defense Advanced Research Projects Agency (DARPA)
Defense Microelectronics Activity (DMEA)
Defense Threat Reduction Agency (DTRA)
Department of Energy (DOE)
Department of Homeland Security
Science and Technology Directorate (DHS/S&T)
Department of Transportation (DOT)
Economic Development Administration (EDA)
Environmental Protection Agency (EPA)
Food and Drug Administration (FDA)
Indian Health Service (IHS)

⁵ iEdison.gov

International Trade Administration (ITA)
National Institute of Food and Agriculture (NIFA)
National Institutes of Health (NIH)
National Institute of Standards and Technology (NIST)
National Oceanic and Atmospheric Administration (NOAA)
National Science Foundation (NSF)
Nuclear Regulatory Commission (NRC)
Office of Naval Research (ONR)
U.S. Agency for International Development (USAID)
United States Forest Service (USFS)

iEdison was created in 1995 in the wake of findings by the Office of Inspector General of the Department of Health and Human Services that the NIH was not sufficiently overseeing and monitoring compliance with Bayh-Dole requirements, including disclosure.⁶

By way of example of how agencies require disclosure, the NIH requires contractors to disclose subject inventions via iEdison, as well as via HHS Form 568, entitled, "Final Invention Statement and Certification (For Grant or Award)," available at: <https://grants.nih.gov/grants/hhs568.pdf>.

The NIH specifies the required information on a FAQ related to the use of iEdison, and also notes that contractors should disclose the subject invention even if they have, in the past, failed to report the invention within the two month period:⁷

5. What information is required to report a subject invention?

The invention disclosure must include the following information:

- Either the EIR Number, Invention Docket Number, or both.
- Invention Title
- Names of all of the inventors and the institutions with which they are associated
- Invention Report Date
- Description of the Invention that must meet the standards set forth per 37 CFR Sec. 401.14 (a)(c)(1):

“ . . . be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of

⁶ <https://oig.hhs.gov/oei/reports/oei-03-91-00930.pdf>

⁷ Available at: https://era.nih.gov/iedison/iedison_faqs.cfm#VIII5 (accessed Jan. 6, 2017).

the invention.”37 C.F.R. 401.14(a)(c)(1)”

-Primary Funding Agency

-All funding agreement numbers and names of the funding agencies

- Any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure

9. If I upload a patent application, can that patent application satisfy the Invention Disclosure Report requirement?

Yes, so long as the EIR Number or Invention Docket Number is included on the submission, the patent record containing the patent/patent application number has been reported in iEdison, and you upload proof that the patent application was filed with the USPTO, e.g., a USPTO submission receipt.

10. What should a grantee/contractor do if a subject invention hasn't been reported to the awarding agency within the required 2 month period?

Always report the invention, even if it is late. The invention report date should be the date the inventor notified the awardee institution of the subject invention. Provide an explanation in the "Explanatory Notes" section of the invention record.

On February 17, 2016, NIH issued a notice entitled “Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison.” The notice explained that failure to disclose the subject invention via both iEdison and Form 568 could result in the loss of rights in the invention.⁸

Finally, under 35 U.S.C. § 202(c)(6) and 37 C.F.R. § 1.77(b)(3), contractors are required to state within the patent application that the federal government contributed funding to support the discovery of the invention and that the government retains certain rights:

35 U.S.C. § 202(c)(6)

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

⁸ National Institutes of Health, Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison, NOT-OD-16-066 (Feb. 17, 2016), NIH Guide Notice, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-066.html>.

(6) An obligation on the part of the contractor, in the event a United States patent application is filed by or on its behalf or by any assignee of the contractor, to include within the specification of such application and any patent issuing thereon, a statement specifying that the invention was made with Government support and that the Government has certain rights in the invention.

35 C.F.R. § 1.77(b)(3)

(b) The specification should include the following sections in order:

...

(3) Statement regarding federally sponsored research or development.

The Manual of Patent Examining Procedure contains the following recommended language:

“This invention was made with government support under (identify the contract) awarded by (identify the Federal agency). The government has certain rights in the invention.”⁹

Remedies for Non-Disclosure

Non-disclosure Permits the Federal Government to Receive Title to the Invention

Failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the Federal Government to **“receive title to any subject invention not disclosed to it within such time”** (emphasis added).

The patent rights clause at 37 C.F.R. § 401.14(a) specifies this right to claim title in subsection (d):

37 C.F.R. § 401.14(a)

(d) Conditions when the Government May Obtain Title

The contractor will convey to the Federal agency, upon written request, title to any subject invention—

(1) If the contractor fails to disclose or elect title to the subject invention within the times specified in (c), above, or elects not to retain title; provided that the agency may only request title within 60 days after learning of the failure of the contractor to disclose or elect within the specified times.

⁹ MPEP (9th ed. Rev. 07.2015, Nov. 2015), § 310.

...

In the past, the Federal Government has utilized its authority to claim title in subject inventions that have not been properly disclosed, as in the case of *Campbell Plastics Engineering & Mfg., Inc. v. Brownlee*, 389 F.3d 1243 (Fed. Cir. 2004) (finding that federal government claim of title in invention was legitimate under federal acquisition regulations and supported by the Bayh Dole Act where disclosure submissions were “piecemeal” and violated the contractual agreement with the government); see also *Central Admixture Pharmacy Services, Inc. v. Advanced Cardiac Solutions, P.C.*, 482 F.3d 1347, 1352-53 (Fed. Cir. 2007) (“Critically, *Campbell Plastics* holds that a Bayh–Dole violation grants the government *discretionary* authority to take title. . . . When a violation occurs, the government can choose to take action; thus, title to the patent may be voidable.”).

In *Campbell Plastics*, the court found that the contract was clear and unambiguous, but moreover the government’s claim to title was “buttressed by the policy considerations behind the Bayh Dole Act.” *Id.* at 1248. These include, specifically under 35 U.S.C. § 200, the need “to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions.”

Correction of the Patent Will Establish Other Enforceable Rights For the Federal Government

Even if the Government permits the continued use of its invention, forcing a correction to the patent will create enforceable obligations and rights designed to protect the public interest. These rights can be used as leverage to force concessions in pricing.

Local Manufacturing

Under 35 U.S.C. § 204, for example, there is a requirement (waivable in individual cases) that the subject invention be manufactured substantially in the United States.¹⁰

35 U.S.C. § 204

Notwithstanding any other provision of this chapter, no small business firm or nonprofit organization which receives title to any subject invention and no assignee of any such small business firm or nonprofit organization shall grant to any person the exclusive right to use or sell any subject invention in the United States unless such person agrees that any products embodying the subject invention or produced through the use of the subject invention will be manufactured substantially in the United States. However, in individual cases, the requirement for such an agreement may be waived by the Federal agency under whose

¹⁰ See also the patents rights clause regarding preference for United States industry at 37 C.F.R. § 401.14(a)(i).

funding agreement the invention was made upon a showing by the small business firm, nonprofit organization, or assignee that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible.

Practical Application

Government rights in a subject invention also implicates the requirement repeated in numerous sections of the Bayh-Dole Act that there be “practical application” of the invention, including once in 35 U.S.C. § 203 on march-in rights, and nine times in 35 U.S.C. § 209 on licensing federally-owned inventions. “Practical application” is defined under 35 U.S.C. § 201(f) to mean “manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized **and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.**” (Emphasis added.)

The phrase “available to the public on reasonable terms” to is a statutory obligation in the Bayh-Dole Act that only has meaning if the invention is available at a reasonable price, and while the NIH has been loath to enforce this requirement, the Congress is increasingly focused on a practical implementation of such an obligation. For example, in 2017, the Senate Armed Services Committee adopted a directive in a committee report to require enforcement of this obligation when the prices of a medical technology were higher in the United States than the median price charged in seven countries with large economies with at least 50 percent of U.S. per capita income.¹¹ There is also U.S. and international case law, as well as statutes in the U.K. and South Africa, defining the phrase “reasonable terms” to include the price of a product of service.¹²

March-In Rights and the Royalty-Free Right

Under 35 U.S.C. § 203(a), the government may require the grant of a license to a third party, or may grant such a license itself, if any of four conditions are met, including the obligation of practical application:

35 U.S.C. § 203

¹¹ 115TH Congress, 1st Session, 2017, Senate Report 115–125. National Defense Authorization Act for Fiscal Year 2018. Report to accompany S. 1519, page 173.

¹² See KEI 10 March 2017 Comments on Army Exclusive License on Zika Virus Vaccine Patents to Sanofi, available at https://www.keionline.org/wp-content/uploads/2017/03/KEI-March_10_2017-3rd-Comments-Zika.pdf.

(a) With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such—

- (1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
- (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
- (3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
- (4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.

The government also retains a perpetual non-exclusive royalty-free license in the invention, written into any funding agreement under 35 U.S.C. § 202(c)(4), and again iterated as a required term and condition for any license of a federally-owned invention under § 209(d)(1). The royalty-free right, as opposed to the march-in rights, has no precondition and can be used at any time, for any reason.

35 U.S.C. § 202

...

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

(4)

With respect to any invention in which the contractor elects rights, the Federal agency shall have a nonexclusive, nontransferrable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world: Provided, That the funding agreement may provide for such additional rights, including the right to assign or have assigned foreign patent rights in the subject invention, as are determined by the agency as necessary for meeting the obligations of the United States under any treaty, international agreement, arrangement of cooperation, memorandum of understanding, or similar arrangement, including military agreement relating to weapons development and production.

35 U.S.C. § 209

...

(d) Terms and Conditions.—Any licenses granted under section 207(a)(2) shall contain such terms and conditions as the granting agency considers appropriate, and shall include provisions—

(1)

retaining a nontransferable, irrevocable, paid-up license for any Federal agency to practice the invention or have the invention practiced throughout the world by or on behalf of the Government of the United States;

...

Both of these rights provide significant leverage to the United States, as they could be used to allow affordable competition. Even the viable threat of use of either of these rights might be sufficient to prompt price reductions or other concessions increasing access while decreasing price.

In some cases there may be more than one patent in a particular medicine, and not all patents may have government rights. In the event that there is at least one patent with government rights, the government could potentially use the royalty-free right in conjunction with the government use provision of 28 U.S.C. § 1498. While § 1498 has been used many times by the military, interest in using the government use law alone on medical technologies has been complicated by uncertainty as to the extent of compensation owed.¹³ Using the royalty-free right and § 1498 together would lessen the amount of compensation owed to the patent holder.

¹³ See, e.g. May 12, 2015 letter from Senator Bernard Sanders to Secretary of the US Department of Veterans Affairs, Robert McDonald.
<https://www.keionline.org/wp-content/uploads/2015/05/12may2015-Sanders-McDonald-Veterans-1498.pdf>; and <https://www.keionline.org/22842>.

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 6/25/2018 5:33:25 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: FR Notice

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, June 25, 2018 1:28 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: FR Notice

b5

From: Berkley, Dale (NIH/OD) [E]
Sent: Monday, June 25, 2018 1:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: FR Notice

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, June 25, 2018 10:12 AM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: FR Notice

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, June 25, 2018 9:27 AM
To: Gottesman, Michael (NIH/OD) [E] <GottesmM@mail.nih.gov>
Cc: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: Re: FR Notice

REL0000024146

b5

Sent from my iPhone

On Jun 25, 2018, at 9:15 AM, Gottesman, Michael (NIH/OD) [E] <gottesmm@mail.nih.gov> wrote:

b5

Michael

From: "Pastan, Ira (NIH/NCI) [E]" <pastani@mail.nih.gov>

Date: Monday, June 25, 2018 at 8:41 AM

To: "Gottesman, Michael (NIH/OD) [E]" <gottesmm@mail.nih.gov>

Subject: Fwd: FR Notice

b5

Ira

Sent from my iPhone

Begin forwarded message:

From: "Lambertson, David (NIH/NCI) [E]" <david.lambertson@nih.gov>

Date: June 25, 2018 at 6:11:16 AM EDT

To: "Pastan, Ira (NIH/NCI) [E]" <pastani@mail.nih.gov>

Subject: RE: FR Notice

Hi Ira,

.

b5

Cheers,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager

REL0000024146

Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702
Bethesda, MD 20892-9702 (USPS)
Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

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From: Pastan, Ira (NIH/NCI) [E]
Sent: Sunday, June 24, 2018 3:21 PM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: Re: FR Notice

Dave.

I gather these objections are now common.

b5

Ira

Ira

Sent from my iPhone

On Jun 24, 2018, at 3:10 PM, Lambertson, David (NIH/NCI) [E]
<david.lambertson@nih.gov> wrote:

Hi Ira,

I got your voicemail from Friday; sorry for the slow response, but I was out of the office and unable to send emails.

So you are aware, we received an objection from KEI, which was cosigned by a couple of other parties. We will review and respond to their comments, and I will keep you updated how things go from there.

Cheers,

From: NIH FOIA [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E734B867D58F45E792D9FA7096AA146D-NIHFOIA]
Sent: 8/28/2017 8:23:48 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Shmilovich, Michael (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7dfe19bfd1d443ceb700b9f22d159a90-shmilovm]; Bordine, Roger (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a44282b444584690bbbe471966f54f1f-bordinerw]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutch]
CC: Thomas, Gina (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a7d21227e5643548f0a7c256b54f83f-gthomas]; Rogers, Karen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b23ef4ca2fa14a6eb174ee611953a396-rogersk]; Burklow, John (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2e57f267323b43c08be856acb5b964ca-burklowj]; NIH FOIA [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e734b867d58f45e792d9fa7096aa146d-nihfoia]
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017
Attachments: Re: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Good afternoon everyone,

After our conference call today,

b5

b5

So please feel free to add or edit out anything in the draft email above.

b5

b5

Thanks everyone.

REL0000024147

Roger Bordine

Program Assistant
Freedom of Information Office
National Institutes of Health
Building 31, Room 5B35
31 Center Drive
Bethesda, MD 20892

Phone: 301-496-5633

Fax: 301-402-4541

Roger.bordine@nih.gov



National Institutes of Health
Turning Discovery Into Health

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 28, 2017 3:10 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>; Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Ok by me

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Monday, August 28, 2017 2:56 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Ok I have a telecon at 15:05 can we gab at 15:30?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 28, 2017 14:56
To: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Cc: Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

I am available the rest of today and tomorrow until 1 pm.

Mark

From: NIH FOIA
Sent: Monday, August 28, 2017 10:32 AM

REL0000024147

To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: Deborah.Kassilke@nih.gov; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Good Morning,

I have not yet responded, and I have cc'd Gina Thomas at OTT FOIA as well. She is handling two FOIA request cases from KEI about CRADA lists and tech transfer records.

Let me know when is best to talk with all of you so we can figure out the best way to respond soon.

Thanks.

Roger Bordine
Program Assistant
Freedom of Information Office
National Institutes of Health
Building 31, Room 5B35
31 Center Drive
Bethesda, MD 20892

Phone: 301-496-5633
Fax: 301-402-4541
Roger.bordine@nih.gov



From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Monday, August 28, 2017 9:52 AM
To: Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>; Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Cc: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>; Deborah.Kassilke@nih.gov; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Roger –

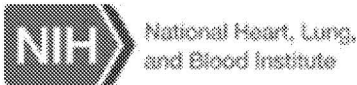
b5

b5

Thank you!!

Michael A. Shmilovich, Esq., CLP

REL0000024147



Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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From: jamespackardlove@gmail.com [<mailto:jamespackardlove@gmail.com>] **On Behalf Of** Jamie Love
Sent: Monday, August 28, 2017 08:28
To: Bordine, Roger (NIH/OD) [E] <roger.bordine@nih.gov>
Cc: Claire Cassedy <claire.cassedy@keionline.org>; NIH FOIA <nihfoia@od.nih.gov>; Deborah.Kassilke@nih.gov;
Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E]
<rohrbaum@od.nih.gov>
Subject: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Dear Roger Bordine,

I am attaching some correspondence I have had the NIH over the issue of CRADAs. When we respond to an NIH request for comments on an exclusive license, we often ask for the CRADA, if any, associated with the license. For example, recently we requested the CRADA associated with the miRecule CRADA, which involves a recent former NIH employee. Typically, as in the case of MiRecule, the NIH licensing officials refuses to give us a copy of the CRADA, claiming it is confidential. We both know that the CRADA document is in fact subject to FOIA, but FOIA takes a long time, can will not be processed before the comment period closes.

When we asked the Office of the Director for a list of all CRADA agreements earlier this year, we were told that the NIH would not provide such a list, because the information was in a computer database and the NIH was not required to create the list from the database under FOIA. We noted at the time that this would force us to FOIA all of the CRADAs, which we thought would be a waste of everyone's time, an opinion that you seemed to share.

Why doesn't the NIH do what some other federal agencies do and list the CRADAs, all of them, on the NIH web page, to enhance the transparency of the licensing and technology transfer operations?

In any event, please decide if the NIH wants to provide a list of the CRADAs or not, and if we have to sue to get copies if you won't in fact provide such a list.

The NIH knows full well the Congress, the press, academic researchers, taxpayer and patient advocacy groups all want to have more transparency of NIH technology transfer activities. The continual stonewalling of legitimate requests for public documents is inappropriate for an agency like the NIH that manages billions of taxpayer dollars to address important health issues, and where the pricing of NIH funded products is a major concern.

In the meantime, please provide KEI with a copy of the miRecule CRADA, and the list of the CRADAs, asap.

James Love
Knowledge Ecology International

Attached are portions of some previous correspondence with the NIH.

REL0000024147

----- Forwarded message -----

From: **NIH FOIA** <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>

Date: Wed, Aug 16, 2017 at 5:15 PM

Subject: RE: Request FOIA Request Re: CRADAs Executed 2010-2017

To: Claire Cassedy <claire.cassedy@keionline.org>

Cc: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>

Good Afternoon,

Thank you for your NIH FOIA request.

Upon reading your request, it appears as though you are asking for all CRADAs from the NIH between 2010-2017, and as it stands, that aspect of your request is too broad and would involve searching records from of all of the 27 institutes and centers at the NIH.

Searching for this many records, and the review efforts afterwards, would put an undue burden on Federal Government resources, as stipulated in the FOIA, and as such, requires you to narrow the scope of your request.

It is estimated that, within your requested timeframe, there would be hundreds of CRADAs across the NIH's institutes, and if you would like to submit a new/revised request detailing a smaller number of specifically named/individual CRADAs, you are more than welcome to request those records. If not, and you would rather request just a list of CRADAs and not the CRADA records themselves, you may do that instead.

Please let us know if you would like to withdraw this initial request in favor of submitting a new request for clarified/named records.

Thank you, and please let us know if you have any questions.

Roger Bordine

Program Assistant

Freedom of Information Office

National Institutes of Health

REL0000024147

Building 31, Room 5B35

31 Center Drive

Bethesda, MD 20892

Phone: 301-496-5633

Fax: 301-402-4541

Roger.bordine@nih.gov

----- Forwarded message -----

From: **James Love** <jamespackardlove@gmail.com>

Date: Thu, Jan 19, 2017 at 7:34 PM

Subject: Re: Your requests for information from NIH OTT

To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@od.nih.gov>

Cc: "Kassilke, Deborah (NIH/OD) [E]" <deborah.kassilke@nih.gov>, "claire.cassedy@keionline.org" <claire.cassedy@keionline.org>

We can't FOIA a database or require records be generated under FOIA. We can FOIA every CRADA, which is what we are going to be forced to do.

But if we knew what records were in the database, a query might save everyone a lot of time.

On Fri, Jan 20, 2017 at 1:07 AM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@od.nih.gov> wrote:

There is no "list" but we do have a database with CRADA and license information.

From: James Love [<mailto:jamespackardlove@gmail.com>]

Sent: Thursday, January 19, 2017 7:01 PM

To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>

Cc: claire.cassedy@keionline.org; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

Subject: Re: Your requests for information from NIH OTT

These are the types of data that make it hard to believe you don't have registry or list of the CRADAs.

<https://www.ott.nih.gov/tt-metrics/crada-metrics>

REL0000024147

On Fri, Jan 20, 2017 at 12:56 AM, James Love <jamespackardlove@gmail.com> wrote:

Thank you.

We do note that the NIH is able to report the total number of CRADAs in any given year, and also that that number is quite a bit smaller than the number of CRADAs noticed in the federal register.

For number of CRADAs, <https://www.ott.nih.gov/ott-statistics>

We are mostly interested in the Standard CRADAs.

We thought if the NIH could provide a count of the number of CRADAs, they must have a registry or list or database that lists the CRADAs, with the name of the CRADA partner and the purpose of the CRADA.

We were surprised when we were told that no such lists exist.

The CRADAs mentioned in the annual reports do not seem inclusive of all CRADAs in a given year.

For example:

In FY15, NIH Institutes executed 5,826 of these collaboration and transfer agreements, including 101 new Cooperative Research and Development Agreements (CRADAs).

I don't think there are 101 CRADAs listed in the annual report, or even the 73 for Standard CRADAs.

So, while the Annual report is useful and interesting, we still don't know who is getting the standard CRADAs.

Also, does the NIH issue exclusive licenses under the CRADAs that are not noticed in the federal register? We were told that the NIH practice was to not provide public notice and comment on all CRADAs and that public notice and comment is not available for all exclusive licenses from CRADAs.

Jamie

REL0000024147

On Fri, Jan 20, 2017 at 12:26 AM, Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov> wrote:

Mr. Love –

Recently your office contact me and two other employees in my office with questions concerning royalty payments, the use of the Federal Registry in tracking NIH CRADAs, and a request for information on the process by which the NIH enters into a CRADA with an industry collaborator. I am aware that Mark Rohrbaugh (cc'd) spoke directly with Claire Cassidy to discuss many of the CRADA related process components including the use of

Federal Register notices and how IP is addressed in a CRADA. If you still have questions regarding the use of CRADAs at NIH, we can certainly schedule another call with you.

I confirmed that the NIH FOIA office is still working on a FOIA request for you concerning royalty payment information. They apologize for the delay, but the FOIA office is short staffed at this time and they are working diligently to hire and train new staff. We just last week brought in an Acting Director for the FOIA office, Katherine Uhl, who is on detail to us from the FDA. She is working diligently to keep the plates spinning and asked that I relay to you they are working on the request. Ms. Uhl invites you to contact her office for a status of your FOIA request if you so desire; that number is 301-496-5633.

I hope that you are aware that our annual reports and statistics can be found on our website in the "MEDIA Room" tab; they may be helpful to you.

Please let me know if you would like another call scheduled with Mark and me; we will gladly set something up.

Deb

Deborah Kassilke

Director, Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

E-Mail:

Deborah.Kassilke@nih.gov

Phone: 301-435-5294

REL0000024147



From: Claire Cassedy [mailto:claire.cassedy@keionline.org]
Sent: Tuesday, August 15, 2017 11:38 AM
To: NIH FOIA <nihfoia@od.nih.gov>
Subject: Request FOIA Request Re: CRADAs Executed 2010-2017

Dear FOIA Officer,

Please find attached a Freedom of Information Act request from Knowledge Ecology International regarding Cooperative Research and Development Agreements executed by the NIH from 2010 to 2017. Thank you in advance for your attention to this request.

Sincerely,

Claire Cassedy

----- Forwarded message -----

From: **Shmilovich, Michael (NIH/NHLBI) [E]** <michael.shmilovich@nih.gov>
Date: Fri, Aug 18, 2017 at 10:34 AM
Subject: FW: miRecule CRADA
To: "jamespackardlove@gmail.com" <jamespackardlove@gmail.com>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutcha@nhlbi.nih.gov>, "Bailey, Brian (NIH/NHLBI) [E]" <bbailey@nhlbi.nih.gov>

Jamie – All scientific, business and financial information pertaining to the CRADA between MiRecule and NIDCD other than what has already been made public by either by publication, published patent applications or other public disclosures, is strictly confidential. As such, we cannot provide you with a copy of that agreement.

Regards,

Michael A. Shmilovich, Esq., CLP

22 August 2017

James Packard Love

Knowledge Ecology International

1621 Connecticut Avenue, Suite 500

Washington, DC 20009

<http://keionline.org>

Work: +1.202.332.2670; Mobile: +1.202.361.3040

james.love@keionline.org

IN RE: 82 Fed. Reg. 36809 (August 7, 2017), "Prospective Grant of Exclusive Patent License: MicroRNA therapeutics for treating squamous cell carcinomas" to miRecule, Inc.

Dear Mr. Love:

....

Dr. Saleh will have direct participation in the research under his company's Cooperative Research and Development Agreement (CRADA) with the National Institute on Deafness and Other Communication Disorders (NIDCD) in order to advance the technology since a positive research outcome under the CRADA is one step closer to the development of a successful therapeutic to at least one squamous cell carcinoma. With respect to your request for various reports including CRADA documents, it is not consistent with our mission to create reports requested by the public and the proprietary content of the agreement governing the CRADA between the NIDCD is strictly confidential. In summary, the CRADA research plan sets forth a joint effort between miRecule and NIDCD to develop chemically modified mimic or mimetic microRNAs that are stable and less susceptible to nuclease degradation than previously identified microRNAs and that serve as therapeutics for cancer when delivered using tumor targeted nanoparticles. The CRADA will test these microRNAs in animal cancer models to evaluate their efficacy and the pharmaceutical properties of candidate formulations.

If your organization requests more documentation, such requests should be filed under the Freedom of Information Act. The webpage for the NIH FOIA Office provides more information on filing requests <http://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedominformation-act-office/submitting-foia-requests>.

Michael A. Shmilovich, Esq., CLP

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: jamespackardlove@gmail.com [jamespackardlove@gmail.com]
on behalf of Jamie Love [james.love@keionline.org]
Sent: 8/28/2017 5:57:01 PM
To: Bordine, Roger (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a44282b444584690bbbe471966f54f1f-bordinerw]
CC: Claire Cassedy [claire.cassedy@keionline.org]; NIH FOIA [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e734b867d58f45e792d9fa7096aa146d-nihfoia]; Kassilke, Deborah (NIH/OD) [E] [Deborah.Kassilke@nih.gov]; Shmilovich, Michael (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7dfe19bfd1d443ceb700b9f22d159a90-shmilovm]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Re: KEI Request FOIA Request Re: CRADAs Executed 2010-2017

Dear Roger Bordine,

Please also provide under FOIA all CRADAs and licenses with Kite Pharma, the company that will be sold to Gilead.

Jamie

On Mon, Aug 28, 2017 at 8:27 AM, Jamie Love <james.love@keionline.org> wrote:
Dear Roger Bordine,

I am attaching some correspondence I have had the NIH over the issue of CRADAs. When we respond to an NIH request for comments on an exclusive license, we often ask for the CRADA, if any, associated with the license. For example, recently we requested the CRADA associated with the miRecule CRADA, which involves a recent former NIH employee. Typically, as in the case of MiRecule, the NIH licensing officials refuses to give us a copy of the CRADA, claiming it is confidential. We both know that the CRADA document is in fact subject to FOIA, but FOIA takes a long time, can will not be processed before the comment period closes.

When we asked the Office of the Director for a list of all CRADA agreements earlier this year, we were told that the NIH would not provide such a list, because the information was in a computer database and the NIH was not required to create the list from the database under FOIA. We noted at the time that this would force us to FOIA all of the CRADAs, which we thought would be a waste of everyone's time, an opinion that you seemed to share.

Why doesn't the NIH do what some other federal agencies do and list the CRADAs, all of them, on the NIH web page, to enhance the transparency of the licensing and technology transfer operations?

In any event, please decide if the NIH wants to provide a list of the CRADAs or not, and if we have to sue to get copies if you won't in fact provide such a list.

The NIH knows full well the Congress, the press, academic researchers, taxpayer and patient advocacy groups all want to have more transparency of NIH technology transfer activities. The continual stonewalling of legitimate requests for public documents is inappropriate for an agency like the NIH that manages billions of taxpayer dollars to address important health issues, and where the pricing of NIH funded products is a major concern.

In the meantime, please provide KEI with a copy of the miRecule CRADA, and the list of the CRADAs, asap.

James Love
Knowledge Ecology International

Attached are portions of some previous correspondence with the NIH.

----- Forwarded message -----

From: **NIH FOIA** <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>
Date: Wed, Aug 16, 2017 at 5:15 PM
Subject: RE: Request FOIA Request Re: CRADAs Executed 2010-2017
To: Claire Cassedy <claire.cassedy@keionline.org>
Cc: NIH FOIA <[nihfoia@od.nih.gov](mailto:.nihfoia@od.nih.gov)>

Good Afternoon,

Thank you for your NIH FOIA request.

Upon reading your request, it appears as though you are asking for all CRADAs from the NIH between 2010-2017, and as it stands, that aspect of your request is too broad and would involve searching records from of all of the 27 institutes and centers at the NIH.

Searching for this many records, and the review efforts afterwards, would put an undue burden on Federal Government resources, as stipulated in the FOIA, and as such, requires you to narrow the scope of your request.

It is estimated that, within your requested timeframe, there would be hundreds of CRADAs across the NIH's institutes, and if you would like to submit a new/revised request detailing a smaller number of specifically named/individual CRADAs, you are more than welcome to request those records. If not, and you would rather request just a list of CRADAs and not the CRADA records themselves, you may do that instead.

Please let us know if you would like to withdraw this initial request in favor of submitting a new request for clarified/named records.

Thank you, and please let us know if you have any questions.

Roger Bordine

Program Assistant

Freedom of Information Office

National Institutes of Health

Building 31, Room 5B35

31 Center Drive

Bethesda, MD 20892

Phone: 301-496-5633

Fax: 301-402-4541

Roger.bordine@nih.gov

----- Forwarded message -----

From: **James Love** <jamespackardlove@gmail.com>

Date: Thu, Jan 19, 2017 at 7:34 PM

Subject: Re: Your requests for information from NIH OTT

To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@od.nih.gov>

Cc: "Kassilke, Deborah (NIH/OD) [E]" <deborah.kassilke@nih.gov>, "claire.cassedy@keionline.org" <claire.cassedy@keionline.org>

We can't FOIA a database or require records be generated under FOIA. We can FOIA every CRADA, which is what we are going to be forced to do.

But if we knew what records were in the database, a query might save everyone a lot of time.

On Fri, Jan 20, 2017 at 1:07 AM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@od.nih.gov> wrote:

There is no "list" but we do have a database with CRADA and license information.

From: James Love [mailto:jamespackardlove@gmail.com]

Sent: Thursday, January 19, 2017 7:01 PM

To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>

REL0000024147.0001

Cc: claire.cassedy@keionline.org; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

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Director, Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

REL0000024147.0001

E-Mail:

Deborah.Kassilke@nih.gov

Phone: 301-435-5294

Cell: b6



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Date: Fri, Aug 18, 2017 at 10:34 AM
Subject: FW: miRecule CRADA
To: "jamespackardlove@gmail.com" <jamespackardlove@gmail.com>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutch@nhlbi.nih.gov>, "Bailey, Brian (NIH/NHLBI) [E]"

REL0000024147.0001

<bbailey@nhlbi.nih.gov>

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Regards,

Michael A. Shmilovich, Esq., CLP

22 August 2017
James Packard Love
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009
<http://keionline.org>
Work: [+1.202.332.2670](tel:+12023322670); Mobile: [+1.202.361.3040](tel:+12023613040)
james.love@keionline.org

IN RE: 82 Fed. Reg. 36809 (August 7, 2017), "Prospective Grant of Exclusive Patent License: MicroRNA

therapeutics for treating squamous cell carcinomas" to miRecule, Inc.

Dear Mr. Love:

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requests <http://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedominformation-act-office/submitting-foia-requests>.

Michael A. Shmilovich, Esq., CLP

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: [+1.202.332.2670](tel:+12023322670), US Mobile: [+1.202.361.3040](tel:+12023613040), Geneva Mobile: [+41.76.413.6584](tel:+41764136584),
twitter.com/jamie_love

--

James Love. Knowledge Ecology International

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twitter.com/jamie_love

From: Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=NIH/NIAID/CN=MMOWATT]
Sent: 2/24/2017 5:11:46 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Lawmakers urge US Army not to issue exclusive license to Sanofi for a Zika vaccine

Thanks – agreed.

May I call you at 11?

Is b6 the best number?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, February 24, 2017 11:57 AM
To: Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Subject: RE: Lawmakers urge US Army not to issue exclusive license to Sanofi for a Zika vaccine

Let's talk Monday morning but generally I think b5

b5

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Friday, February 24, 2017 11:47 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Subject: Lawmakers urge US Army not to issue exclusive license to Sanofi for a Zika vaccine

Hi Mark,

I hope all's well!

I'm sure that you're well aware of this situation.

b5

 and we
thing it's important to provide him with briefing materials on this subject. b5

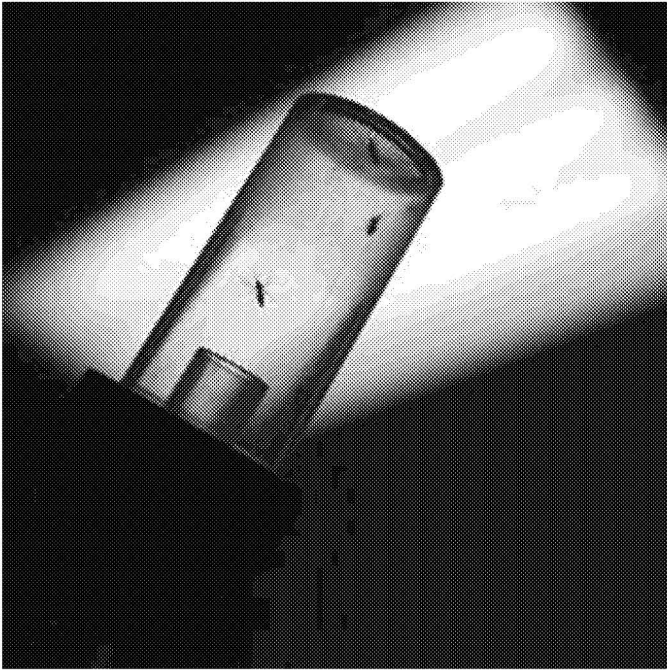
b5

I'm tied up today, but if you prefer to talk I can be available on Monday morning.

Thanks for sharing your thoughts.

Mike

Lawmakers urge US Army not to issue exclusive license to Sanofi for a Zika vaccine



John Moore/Getty Images Mosquitos caught for testing for

Zika and other mosquito-borne diseases.

By Ed Silverman @Pharmalot

February 22, 2017

Nearly a dozen members of Congress are urging the US Army not to issue an exclusive license to Sanofi Pasteur to develop a vaccine for the Zika virus over concerns the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

“In order to ensure that the investment made by taxpayers was worthwhile, it is critical that we ensure the vaccine to prevent against the Zika virus is accessible to anyone who requires it,” the lawmakers wrote on Wednesday in a letter to Robert Speer, the Acting Secretary of the Army.

But if the Army does proceed, the lawmakers implored Speer to issue a limited license and impose requirements that allow the federal government to intervene if the drug maker sets a price that “would make it accessible to millions of Americans who need access to a vaccine they paid to develop.” The letter was signed by 11 House Democrats.

The move comes after the military last December revealed plans to award the company a license to a pair of government patents. That followed months of mounting alarm among public health officials over the spread of Zika, the mosquito-borne virus that can cause birth defects. At the same time, there is speculation that the market for such a vaccine may become quite lucrative.

The government, however, has not disclosed specifics about the license. We do know that Sanofi Pasteur, which is one of the world’s biggest vaccine makers and a unit of the French pharmaceutical company, was awarded a \$43.2 million grant by the Biomedical Advanced Research and Development Authority and also has a co-development deal with the Walter Reed Army Institute of Research.

The lack of information prompted advocacy groups to complain to the Army, expressing concerns that the vaccine may be priced out of reach for many Americans, who helped fund the invention in the first place.

A Zika vaccine is being developed at warp speed, but will there be a market for it?

For instance, Knowledge Ecology International, a group that tracks access to medicines, asked the Army Medical Research and Materiel Command for information about the terms, such as how long the license would run, how much the government has spent, royalty rates, and pricing. The group made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit.

A KEI spokesman says request for information have not yet been fulfilled.

In comments filed last month to the US Army, Doctors Without Borders argued that an exclusive license will give Sanofi “a monopoly in the research, manufacturing and sale of the technology.” The advocacy group added that an exclusive license is no guarantee that all populations in need will be served and that Sanofi would be free to market to the most profitable markets.

We asked the US Army for comment and will update you accordingly.

A Sanofi Pasteur spokeswoman wrote us that the company is “well positioned” to clinically develop the vaccine and is “capable of making it available to those areas that need it most.” She also repeated what was told us two months ago — the vaccine maker has not yet created a specific commercial plan and could not say what price may eventually be charged or when the vaccine might become available. Late-stage testing has not begun. She did say the company expects to ask BARDA for more funding.

In a recent email exchange, Rachel Sachs, an associate professor at the Washington University School of Law, wrote us that “Sanofi may also gain additional collateral benefits associated with the vaccine that make [the] argument [by the advocacy groups] even stronger. The government may choose to stockpile doses of the vaccine, or purchase it in bulk for military service members overseas. Where the government is acting as purchaser, the ‘paying twice’ argument becomes clear: the government is paying for the clinical trials and may later be purchasing the vaccine at a monopoly price.”

Michael R. Mowatt, Ph.D.
Director, Technology Transfer and Intellectual Property Office

National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services

+1 301 496 2644



The information in this e-mail and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the original intended recipient. If you have received this e-mail in error please inform the sender and delete it from your mailbox or any other storage devices. National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From: Yang, Jasmine (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCACD5B675E74725A0D6A6FC9A130431-YANGJJ2_6B5]
Sent: 1/2/2019 6:37:45 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: KEI comment to intent to grant A-066-2019
Attachments: Re: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof"; Ltr to KEI_2019-01-02.docx

Hello,

I have received the attached emails from Jaime Love of KEI in response to the following FRN
<https://www.federalregister.gov/documents/2018/12/21/2018-27671/prospective-grant-of-an-exclusive-patent-license-multifunctional-rna-nanoparticles-and-methods-of-uses>.

Attached is a draft response that I intend to respond with, pending your comments/feedback. Please let me know if anything needs to be changed to the draft and if you have any questions regarding the company, Sixfold, or the technology.

Thank you,
Jasmine

Jasmine J. Yang, Ph.D.
Sr. Technology Transfer Manager
Technology Transfer Center | National Cancer Institute | The National Institutes of Health
Riverside 5, Suite 400 | 3490 Progress Drive | Frederick, MD 21701
Email: jasmine.yang@nih.gov | (P) 301-624-8775 | (Fax) 301-631-3027
<https://techtransfer.cancer.gov/>

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited. Please notify me and delete the original and all copies of this communication immediately.

From: James Love [james.love@keionline.org]
Sent: 12/25/2018 2:52:44 PM
To: Yang, Jasmine (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcacd5b675e74725a0d6a6fc9a130431-yangjj2_6b5]
Subject: Re: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof"
Flag: Follow up

Also, can you explain why the NIH believes an exclusive license is necessary for this invention, since it appears to related to editing technologies or delivery mechanisms for drugs.

Jamie

On Tue, Dec 25, 2018 at 9:46 AM James Love <james.love@keionline.org> wrote:
Dear Jasmine Yang,

Can I have a copy of any unpublished patent applications for this federal register notice?

<https://www.federalregister.gov/documents/2018/12/21/2018-27671/prospective-grant-of-an-exclusive-patent-license-multifunctional-rna-nanoparticles-and-methods-of>

Requests for copies of the patent application, inquiries, and comments relating to the contemplated an Exclusive Patent License should be directed to: Jasmine Yang, Sr. Licensing and Patenting Manager, NCI Technology Transfer Center, 9609 Medical Center Drive, RM 1E530 MSC 9702, Bethesda, MD 20892-9702 (for business mail), Rockville, MD 20850-9702 Telephone: (240)-276-5530; Facsimile: (240)-276-5504 Email: jasmine.yang@nih.gov.

--

James Love. Knowledge Ecology International
<http://www.keionline.org>
twitter.com/jamie_love

--

James Love. Knowledge Ecology International
<http://www.keionline.org>
twitter.com/jamie_love



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health/ NCI
8490 Progress Drive
Riverside 5 building, Suite 400
Frederick, MD 21701
Phone (301) 624-8775
FAX (301) 631-3033

via email only

January 2, 2019

Mr. James Love, Knowledge Ecology International
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009

IN RE: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof", [Federal Register / Vol. 83, No. 245 / Friday, December 21, 2018 / Notices]

Dear Mr. Love:

Thank you for providing me with your comments regarding the above-referenced Federal Register Notice of the proposed license the National Cancer Institute intends to grant to Sixfold Biosciences Inc. The notice period provides an opportunity for public comment and possible objection to the proposed license. We consider all comments prior to negotiating the proposed license and have considered your comments.

With respect to your comment regarding use of the technologies in gene-editing or drug delivery, prior to posting a notice for a proposed grant of an exclusive license, the NIH has determined that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) have been satisfied and that the company is qualified both technically and financially to be granted an exclusive license to the Government's intellectual property in the fields of use as specified. The technologies have broad capabilities and as such, additional fields of use are available for licensing.

With regards to your request for unpublished patent application, all relevant patent application information are publicly available and can be found at the USPTO Public Pair or WIPO databases.

Sincerely,

Jasmine Yang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Centerd

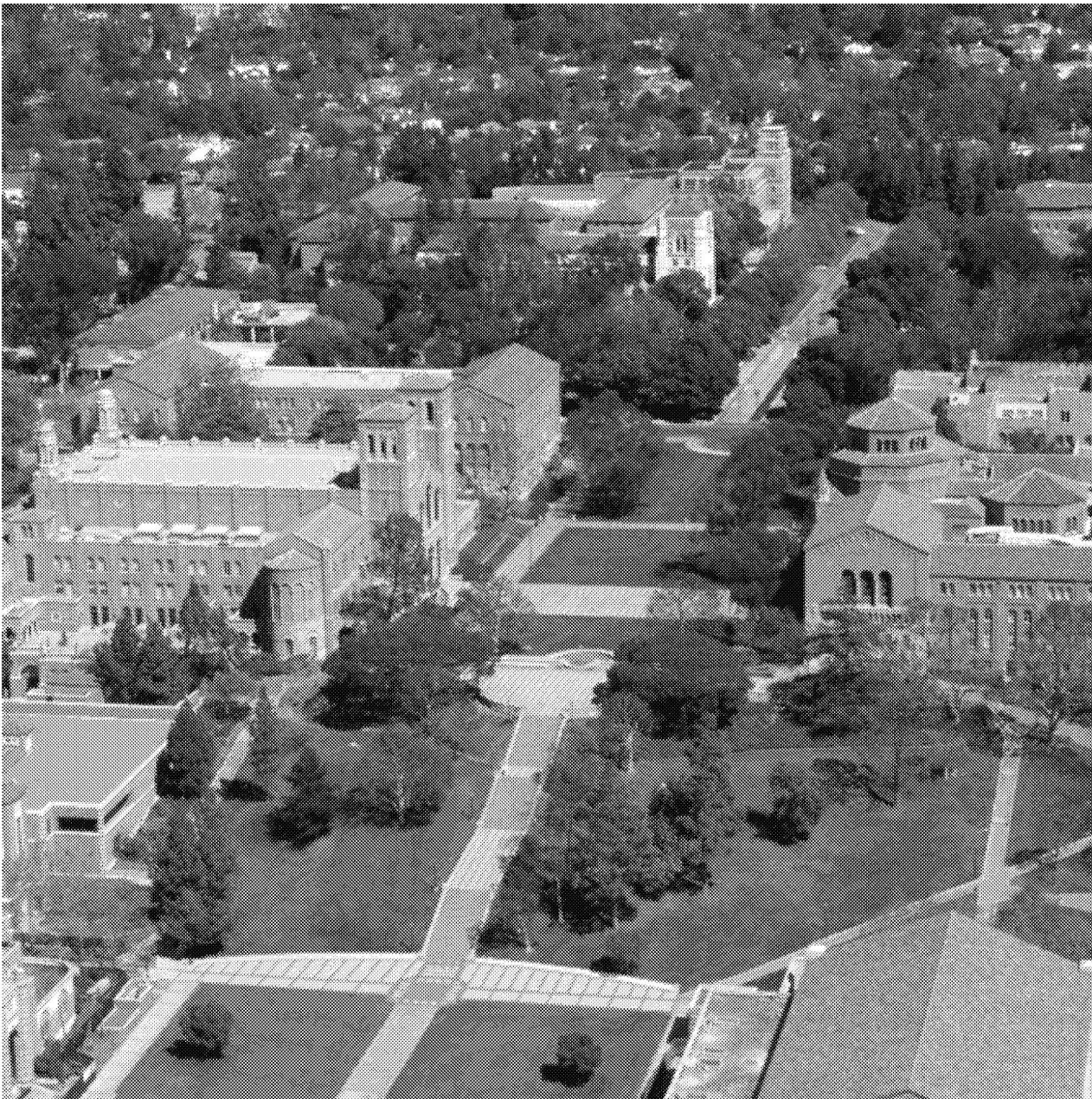
REL0000024151.0002

From: Wojtowicz, Emma (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=45C6610ACA6E44A08D497630425E5ECD-WOJTOWICZEM]
Sent: 4/3/2018 12:41:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: UCLA Students, & Xtandi Drug Patents

Students push UCLA to improve access to a cancer drug developed by its scientists

By [ELIZABETH COONEY](#) [@cooney_liz](#)
MARCH 30, 2018

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A view of

UCLA's campus. [UCLA](#)

S

tudents at UCLA are calling on the university to ease access to a prostate cancer drug developed on campus.

The drug, Xtandi, is at the center of a legal battle in India over whether generic competitors can enter the market — a battle in which, students say, the university is on the wrong side.

“Lives are at stake and UCLA can and must live up to its mission as a public research university,” Universities Allied for Essential Medicines wrote in a petition to the university system’s president, Janet Napolitano, earlier this month. “By filing this patent claim, UCLA is actively complicit in creating access barriers that are causing harm to prostate cancer patients worldwide.”

In addition to urging the university to drop its patent claim, signatories are asking it to adhere to licensing guidelines adopted in 2009 “to implement global access licensing that would ensure that medications and medical innovations developed at UCLA are accessible [and] affordable in low and middle income countries.”

The [petition](#) has so far garnered 210 signatories.

TRENDING

They built a game-changing cancer-killing therapy. Now they're taking on a new kind of CAR-T therapy

The campaign follows similar movements by students pressuring universities in recent years. In 2015 UAEM and public health groups coordinated a [campaign against Johns Hopkins University](#) to keep tuberculosis drugs affordable. Last year, Hopkins signed a license with the [Medicines Patent Pool](#), a U.N.-backed organization, to make its experimental TB drug sutezolid available royalty-free in certain cases.

And in 2001, a group of [Yale students working with Médecins Sans Frontières](#) prevailed on Yale and Bristol-Myers Squibb to allow a generic version of a Yale-developed HIV/AIDS drug to be made in sub-Saharan Africa.

In the case of Xtandi, the drug was discovered at UCLA with National Institutes of Health funding. In 2005 UCLA licensed the drug to Medivation, which marketed the drug in a partnership with Astellas Pharmaceuticals. Medivation was sold to Pfizer in 2016.

The university sold its share of the royalty rights in 2016 to the investment firm Royalty Pharma for \$1.14 billion, \$520 million of which went to UCLA. While it no longer collects royalties, UCLA retains partial ownership of the patent on the chemical compound that later became Xtandi.

Now UCLA, Astellas, and Medivation are pursuing a patent for Xtandi in India to protect it from potential competition. One attempt to gain a patent has been denied by the Indian Patent Office, but that decision is being appealed.

Related Story:

Just when can NIH override a patent for a high-priced drug?

“I think the university’s patent management is very much a public health issue,” said Kayla Gu, a medical student at UCLA involved in the protest who spoke about the issue at a board of regents meeting earlier this month. “This is a very typical case where tax-funded drugs are licensed to the pharmaceutical industry, and what happens to drugs afterward is under very little supervision — even though the drug is supposed to be owned by the public.”

The university did not immediately respond to a request for comment.

UAEM was joined by two other advocacy groups in signing the UCLA petition: the Union for Affordable Cancer Treatment and Knowledge Ecology International.

In Washington, Knowledge Ecology International has also pressed federal officials to act on rising drug prices. The group has urged the [NIH](#) and the Department of Health and Human Services to

invoke a march-in right to override some drug patents. A law passed in 1980 says a federal agency that funds private research can require a drug maker to license its patent to another party in order to “alleviate health and safety needs which are not being reasonably satisfied” or when the benefits of a drug are not available on “reasonable terms.”

The UCLA students and the activist groups working with them say high drug prices would qualify for march-in rights, in the U.S. and other countries. Gu said they want to make sure the university licenses its drugs in a way that protects the interests of patients and the public.

“As medical students, we feel almost personally responsible,” Gu said.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, April 2, 2018 6:38 PM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: FW: UCLA Students, & Xtandi Drug Patents

Could you send me a copy of this article please. Thx

From: Koniges, Ursula (NIH/OD) [E]
Sent: Monday, April 02, 2018 9:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Dodson, Sara (NIH/OD) [E] <sara.dodson@nih.gov>
Subject: UCLA Students, & Xtandi Drug Patents

STAT Plus article of interest:

Students Push UCLA To Improve Access To Drug Developed By Its Scientists. STAT Plus (3/30, Cooney, Subscription Publication, 32K) reported that UCLA students are pushing the university to ease access over Xtandi, a prostate cancer drug that was developed on campus with National Institutes of Health funding. The students are urging the university to drop its patent claim in a legal battle in India. In their petition to the system’s president, Janet Napolitano, Universities Allied for Essential Medicines wrote, “Lives are at stake and UCLA can and must live up to its mission as a public research university.”

From: Plude, Denise (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=91F83D681D984EAA8FE3DE287AEBFA01-PLUDEDE]
Sent: 11/27/2017 4:10:47 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: WF 368759 - due 11/27
Attachments: 1 HHS, Penn CAR T patent disclosures 17 Oct 2017, final.pdf; 2 ForwardedAttachment_1.txt; 3 ForwardedAttachment_2.html.docx; 4 Email 00388988 16 11 2017.pdf; Request to Investigate U Penn Failure to Disclose Federal Funding of CAR T Patents; Rnd1 DRAFT RESPONSE to KEI 11202017ah_pj.docx

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, November 27, 2017 11:10 AM
To: Plude, Denise (NIH/OD) [E] <pludedede@mail.nih.gov>
Subject: RE: WF 368759 - due 11/27

Can you send me the document please

From: Plude, Denise (NIH/OD) [E]
Sent: Monday, November 27, 2017 9:50 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: WF 368759 - due 11/27
Importance: High

Please remember to write out the suggested changes by identifying page, paragraph, and sentence numbers. DDRMS does not recognize colors and strikeouts.

From: Plude, Denise (NIH/OD) [E]
Sent: Monday, November 27, 2017 8:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: WF 368759 - due 11/27
Importance: High

Mark, please send the final edits to respond by noon today for Lyric to review.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, November 22, 2017 12:32 PM
To: Jorgenson, Lyric (NIH/OD) [E] <lyric.jorgenson@nih.gov>
Cc: Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>; Plude, Denise (NIH/OD) [E] <pludedede@mail.nih.gov>; Fennington, Kelly (NIH/OD) [E] <fenningk@od.nih.gov>; Ampey, Bryan (NIH/OD) [E] <bryan.ampey@nih.gov>
Subject: Re: WF 368759 - due 11/27

Change looks good

Sent from my iPhone

On Nov 22, 2017, at 12:27 PM, Jorgenson, Lyric (NIH/OD) [E] <lyric.jorgenson@nih.gov> wrote:

review.

REL0000024155



1621 Connecticut Ave NW Suite 500
Washington, D.C. 20009
+1 (202) 332-2670
<http://keionline.org>

October 16, 2017

The Honorable Eric D. Hargan
Acting Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Via: eric.hargan@hhs.gov

Re: The failure of the University of Pennsylvania to disclosure the NIH interest in five CAR T patents

Dear Secretary Hargan:

This letter requests that you investigate substantial evidence that the Trustees of the University of Pennsylvania ("UPenn") failed to satisfy disclosure requirements under the Bayh-Dole Act, 35 U.S.C. §§ 200 *et seq.*, and federal regulations, 37 C.F.R. §§ 401.3(a) & 401.14, with regard to federally-funded subject inventions related to chimeric antigen receptor T cell ("CAR T") therapy in human cancers such as hematologic malignancies, embodied in the following U.S. Patent Nos.:

8,916,381 (the "381 patent")
8,975,071 (the "071 patent")
9,102,760 (the "760 patent")
9,101,584 (the "584 patent")
9,102,761 (the "761 patent")

We have a high degree of confidence that these five patents (collectively, the "2014 patents") are subject inventions under the Bayh-Dole Act, in that they were "conceived or first actually reduced to practice in the performance of work under a funding agreement." 35 U.S.C. § 201(e).

In spite of the significant federal funding supporting the chimeric antigen receptor research at UPenn, none of the 2014 patents list government rights in the invention, nor the role of National Institutes of Health (NIH) grants in the development of the CAR T technology.

The 13 patents sharing the same 5 inventors

Table 1 provides information on 13 granted patents that mention “chimeric antigen receptor”, are assigned to the Trustees of the University of Pennsylvania, and which have the same 5 inventors — all current or former employees of the University of Pennsylvania.

For these 13 patents, there are 5 and only 5 inventors mentioned on the patent.

- The four patents filed from June 2012 to December 2013 disclosed several NIH grants and federal government rights in the patent.
- The five patents filed from August to December 2014 disclosed no federal funding.
- The four patents filed from December 2015 to January 2016 also disclosed NIH grants and federal government rights in the patents.

The five patents of interest are those filed between August and December 2014 which share the exact same inventors and the exact same earliest priority date. We believe these 5 patents failed to disclose federal rights in the patents.

Table 1: UPenn CAR Patents with the Five Main Inventors

Patent Number	NIH Grants	Date filed	Earliest priority date	Carl H June	Michael D Kalos	Bruce L Levine	Michael C Milone	David L Porter
9,499,629	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2012-06-14	2010-12-09	Y	Y	Y	Y	Y
8,906,682	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2013-07-10	2010-12-09	Y	Y	Y	Y	Y
8,911,993	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482	2013-07-10	2010-12-09	Y	Y	Y	Y	Y

9,328,156	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2013-12-16	2010-12-09	Y	Y	Y	Y	Y
8,916,381	None reported	2014-08-22	2010-12-09	Y	Y	Y	Y	Y
8,975,071	None reported	2014-08-22	2010-12-09	Y	Y	Y	Y	Y
9,102,760	None reported	2014-12-11	2010-12-09	Y	Y	Y	Y	Y
9,101,584	None reported	2014-12-12	2010-12-09	Y	Y	Y	Y	Y
9,102,761	None reported	2014-12-12	2010-12-09	Y	Y	Y	Y	Y
9,481,728	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2015-12-30	2010-12-09	Y	Y	Y	Y	Y
9,464,140	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2016-01-14	2010-12-09	Y	Y	Y	Y	Y
9,540,445	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2016-01-14	2010-12-09	Y	Y	Y	Y	Y
9,518,123	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2016-01-15	2010-12-09	Y	Y	Y	Y	Y

There is one additional relevant patent that has three of the same five inventors, was filed January 15, 2016, and that disclosed funding from six NIH grants.

Table 2: The CAR Patent with 3 of the 5 Inventors

Patent Number	NIH Grants	Date filed	Earliest priority date	Carl H June	Michael D Kalos	Bruce L Levine	Michael C Milone	David L Porter
9,572,836	K24CA11787901, 1R01CA120409, 1R01CA105216, R01AI057838, R01113482** and 1PN2EY016586	2016-01-15	2012-07-13	Y	Y	Y		

We believe that the 2014 patents, which share the exact same inventors and the exact same earliest priority date, have failed to disclose NIH funding and acknowledge U.S. governmental rights in the patents.

Furthermore, we submit evidence, presented below, that the NIH itself has identified at least three NIH grants as related to each of the five 2014 patents.

Why disclosure is important

CAR T technology is a critical development for immunotherapy that relies on the patient's own cells for the treatment of cancer. This type of treatment holds great promise, with multiple companies including, but not limited to, Novartis, Juno, and Gilead focused on bringing products to market.

There is a concern is that CAR T patents will be used to block innovation by competitors. The relationship between Novartis and UPenn suggests commercial interests will play an important role in enforcing any granted patents. The past litigation involving UPenn, Juno, St Jude's Hospital and others is an early indication there are overlapping claims on CAR T patents and the potential for future litigation. In the past, aggressive litigation by Novartis over Chiron patents on the hepatitis C virus delayed introduction of new drugs by several years. After the announcement that Gilead would acquire Kite Pharma, Gilead indicated to KEI that it expects considerable litigation over CAR T patent claims, in part due to overlapping claims.

The pricing of CAR T treatments will be high when monopolies persist. Novartis's opening price of \$475,000 per treatment for Kymriah¹ is an early indication that CAR T prices will be aggressive, placing burdens on Medicare, Medicaid and other federal programs, as well as the private sector payers.

When the federal government has rights in patents under the Bayh-Dole Act, there are opportunities to force less restrictive licensing, as was done on the WARF patents on stem cells and the patents on vaccine manufacturing technologies using reverse genetics.

The Bayh-Dole Act also requires federally-funded inventions to be made "available to the public on reasonable terms."

¹ Gina Kolata, "New Gene-Therapy Treatments Will Carry Whopping Price Tags," *New York Times*, September 11, 2017. Available at <https://www.nytimes.com/2017/09/11/health/cost-gene-therapy-drugs.html>

I. The Bayh-Dole Act Requires Disclosure of Government Rights in Subject Inventions

The Bayh-Dole Act and federal regulations and guidelines make clear several obligations for contractors in the disclosure of government rights in subject inventions, including: (1) a requirement to disclose that federal funding contributed to an invention; (2) NIH contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

First, contractors are required to disclose subject inventions discovered with federal funding in a timely manner and with sufficient detail to describe the invention.

Under 35 U.S.C. § 202(c)(1), any contractor that receives funding from the federal government is required to "disclose each subject invention to the Federal agency within a reasonable time after it becomes known to contractor personnel responsible for the administration of patent matters."

The statute defines a "subject invention" at 35 U.S.C. § 201(e) as "any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement," and defines a contractor at 35 U.S.C. § 201(c) as "any person, small business firm, or nonprofit organization that is party to a funding agreement."

"Funding agreement" is defined at 35 U.S.C. § 201(b) to mean "any contract, grant, or cooperative agreement entered into between any Federal agency, other than the Tennessee Valley Authority, and any contractor for the performance of experimental, developmental, or research work funded in whole or in part by the Federal Government."

Under 37 C.F.R. § 401.3(a), each federal funding agreement shall contain the "standard patent rights clause" found at 37 C.F.R. § 401.14(a), barring specific circumstances and exceptions.² Subsection (c)(1) of the patent rights clause outlines the disclosure requirements, including a two month time limit on the disclosure of patents and a requirement that the disclosure have sufficient detail:³

37 C.F.R. § 401.14(a)(c)(1)

(c) Invention Disclosure, Election of Title and Filing of Patent Application by *Contractor*

² The exceptions do not contain reference to the disclosure requirements.

³ Italics in original.

(1) The *contractor* will disclose each subject invention to the *Federal Agency* within two months after the inventor discloses it in writing to *contractor* personnel responsible for patent matters. The disclosure to the *agency* shall be in the form of a written report and shall identify the contract under which the invention was made and the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the invention. The disclosure shall also identify any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure. In addition, after disclosure to the *agency*, the *Contractor* will promptly notify the *agency* of the acceptance of any manuscript describing the invention for publication or of any on sale or public use planned by the *contractor*.

...

(4) Requests for extension of the time for disclosure, election, and filing under subparagraphs (1), (2), and (3) may, at the discretion of the *agency*, be granted.

Second, in implementing this regulation, the NIH requires contractors to disclose subject inventions via iEdison, an online electronic system for reporting inventions and patents discovered under federal grants, and via HHS Form 568, entitled, "Final Invention Statement and Certification (For Grant or Award)," available at: <https://grants.nih.gov/grants/hhs568.pdf>.

The NIH specifies the required information on an FAQ related to the use of iEdison, and also notes that contractors should disclose the subject invention even if they have, in the past, failed to report the invention within the two month period:⁴

iEdison & Intellectual Property FAQs and Resources

5. What information is required to report a subject invention?

The invention disclosure must include the following information:

- Either the EIR Number, Invention Docket Number, or both.
- Invention Title
- Names of all of the inventors and the institutions with which they are associated
- Invention Report Date

⁴ Available at: https://era.nih.gov/iedison/iedison_faqs.cfm#VIII5 (accessed Oct. 10, 2017).

-Description of the Invention that must meet the standards set forth per 37 CFR Sec. 401.14(a)(c)(1):

“ . . . be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the invention.”37 C.F.R. 401.14(a)(c)(1)”

-Primary Funding Agency

-All funding agreement numbers and names of the funding agencies

- Any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure

9. If I upload a patent application, can that patent application satisfy the Invention Disclosure Report requirement?

Yes, so long as the EIR Number or Invention Docket Number is included on the submission, the patent record containing the patent/patent application number has been reported in iEdison, and you upload proof that the patent application was filed with the USPTO, e.g., a USPTO submission receipt.

10. What should a grantee/contractor do if a subject invention hasn't been reported to the awarding agency within the required 2 month period?

Always report the invention, even if it is late. The invention report date should be the date the inventor notified the awardee institution of the subject invention. Provide an explanation in the "Explanatory Notes" section of the invention record.

On February 17, 2016, the NIH issued a notice entitled “Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison.” The notice explained that failure to disclose the subject invention via both iEdison and Form 568 could result in the loss of rights in the invention.⁵ As explained below in section V on remedies, this notice is consistent with precedent related to failure to disclose.

Finally, under 35 U.S.C. § 202(c)(6) and 37 C.F.R. § 1.77(b)(3), contractors are required to state within the patent application that the federal government contributed funding to support the discovery of the invention and that the government retains certain rights:

⁵ National Institutes of Health, Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison, NOT-OD-16-066 (Feb. 17, 2016), NIH Guide Notice, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-066.html>.

35 U.S.C. § 202(c)(6)

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

(6) An obligation on the part of the contractor, in the event a United States patent application is filed by or on its behalf or by any assignee of the contractor, to include within the specification of such application and any patent issuing thereon, a statement specifying that the invention was made with Government support and that the Government has certain rights in the invention.

35 C.F.R. § 1.77(b)(3)

(b) The specification should include the following sections in order:

...

(3) Statement regarding federally sponsored research or development.

The Manual of Patent Examining Procedure contains the following recommended language:

“This invention was made with government support under (identify the contract) awarded by (identify the Federal agency). The government has certain rights in the invention.”⁶

II. UPenn Failed to Disclose the 2014 Patents as Subject Inventions Under the Bayh-Dole Act

UPenn received substantial federal funding from the NIH for the development of CAR T technology

Seven grants from the NIH between the years of 1995 and 2017 helped push UPenn to the forefront of research institutions working on the development of CAR T technology.

⁶ MPEP (9th ed. Rev. 07.2015, Nov. 2015), § 310.

Table 3a: NIH Grants to UPenn Relating to CAR T Technology

NIH Grant	Grant Period	Grant Title	Patents	Grant Recipient	Grant Amount
1R01CA105216	2004	CULTURE SYSTEMS TO PROPOGATE [sic] HUMAN T CELL SUBSETS	12	JUNE, CARL H.	\$286,100
1R01CA120409	2006	IMMUNOTHERAPY OF MESOTHELIN EXPRESSING TUMORS WITH LENTIVIRAL ENGINEERED T CELLS	2	JUNE, CARL H.	\$278,675
R01CA120409	2006-2016	IMMUNOTHERAPY WITH CAR T CELLS/ IMMUNOTHERAPY OF MESOTHELIN EXPRESSING TUMORS WITH LENTIVIRAL ENGINEERED T CELLS	10	JUNE, CARL H.	\$2,676,065
K24CA11787901	2006	MID-CAREER INVESTIGATOR AWARD IN ALLOGENEIC ADOPTIVE IMMUNOTHERAPY	9	PORTER, DAVID	\$155,592
R01CA172921	2013-2017	USE OF GENETICALLY ENGINEERED T CELLS TARGETING TUMOR STROMA TO TREAT LUNG CANCER	1	ALBELDA, STEVEN MARK	\$1,177,634
R01AI057838	2004-2008	REGULATION OF HUMAN T CELL ACTIVATION BY THE CD28 FAMILY	12	RILEY, JAMES L	\$1,731,361
P01CA66726	1995-2016	IMMUNO/IMMUNO-GENE THERAPIES FOR THORACIC MALIGNANCIES, GENE THERAPY FOR MALIGNANT MESOTHELIOMA	1	ALBELDA, STEVEN MARK et al.	\$22,203,754

In addition, the University of Pennsylvania was co-recipient of one grant with the Wistar Institute:

Table 3b: NIH Grants to UPenn as Co-Recipient Relating to CAR T Technology

NIH Grant	Grant Period	Grant Title	Patents	Grant Recipient	Grant Amount
CA141144	2010-2014	FIBROBLAST ACTIVATION PROTEIN IN THE TUMOR MICROENVIRONMENT IN LUNG CANCER	1	PURE', ELLEN	\$1,573,613

UPenn is the currently the assignee of twenty-nine patents relating to CAR technology

As of the date of this letter, the Trustees of the University of Pennsylvania is the assignee of twenty-nine US patents that include the term "chimeric antigen receptors." The filing dates for the patents are from February 4, 2011 to January 15, 2016. The patents were granted from December 23, 2014 to October 10, 2017.

Thirteen of the twenty-nine patents share the same five inventors, including the 2014 patents

As described at the outset, thirteen of the twenty-nine patents list the same five inventors: Carl H June, Michael D Kalos, Bruce L Levine, Michael C Milone, and David L Porter. A fourteenth patent omits Milone and Porter as inventors, while June, Kalos and Levine remain listed.

As shown in Table 1, of these particular patents with the same five inventors, only the 2014 patents fail to disclose the NIH grants that supported the invention.

Note that of the thirteen patents with the five main inventors, all except the 2014 patents refer to the same grants: K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**. The fourteenth patent (with three of the five inventors) discloses these same grants in addition to NIH grant 1PN2EY016586.

All thirteen of the patents with these five main inventors have patents with the same earliest priority date of December 09, 2010. The 2014 patents in particular were filed on August 22 and December 12 of 2014.

The inventors of the 2014 patents

Carl H. June, M.D.

Carl H. June is the Richard W. Vague Professor in Immunotherapy, Director of the Center for Cellular Immunotherapies, and Director of the Parker Institute for Cancer Immunotherapy at the University of Pennsylvania's Perelman School of Medicine. He is the director of Translational Research at the Abramson Cancer Center as well as as an investigator of the Abramson Family Cancer Research Institute. His lab researches and develops CARs and the means to deliver them into human T cells.⁷ Dr. June has been examining T cell systems and CAR therapies for several decades, and has published extensively on the topics. In July 2014, his lab's CAR T approach to cancer immunotherapy received US FDA Breakthrough Therapy designation, the first academic research center to received such a recognition. In 2017 Dr. June received the

⁷ <http://www.med.upenn.edu/apps/faculty/index.php/g275/p2328>

David A. Karnofsky Memorial Award for his role in developing engineered T cells in targeted cancer therapy. Dr. June became tenured faculty at UPenn in 1999.⁸

Michael D. Kalos, PhD

Michael D. Kalos is the Chief Scientific Officer in Cancer Immunobiology at Eli Lilly and Company, but was a faculty member at the University of Pennsylvania from 2008 to 2013, where he established the Translational and Correlative Studies Laboratory within the Perelman School of Medicine.⁹

Michael Milone

Michael Milone is an Associate Professor of Pathology and Laboratory Medicine at the Hospital of the University of Pennsylvania and Perelman School of Medicine.¹⁰ Milone's LinkedIn entry notes that as a postdoctoral fellow working with Dr. Carl June, Milone "designed CTL019 (TN: Kymriah, INN: tisagenlecleucel), a CD19-specific T cell immunotherapy, and conducted the IND-enabling, pre-clinical studies of this novel genetically-engineered cell therapy required for the initial Phase I clinical trial."¹¹ His current research includes, "developing chimeric antigen receptors (CARs) for adoptive immunotherapy of cancer with enhanced function and improved safety, developing and applying synthetic immunoreceptors to the treatment of immune-mediated disease, and exploring the role of co-stimulatory signals in directing T cell metabolism and the way this metabolism affects T cell function within tumors."¹² Dr. Milone has been with the University since 1999.¹³

Bruce Levine

Dr. Bruce Levine is a Barbara and Edward Netter Professor in Cancer Gene Therapy, and is the Founding Director of the Clinical Cell and Vaccine Production Facility (CVPF) in the Department of Pathology and Laboratory Medicine and the Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, and has been with the University since 1999.¹⁴ Dr. Levine lists "good manufacturing practices" as an area of expertise in his biography on the UPenn website.¹⁵

⁸ <http://www.aacr.org/Funding/Pages/su2c-cri-committee-detail.aspx?ItemID=2#.Wd0TLUuGPq6>

⁹ <https://www.linkedin.com/in/michael-kalos-81366b9>

¹⁰ <http://pathology.med.upenn.edu/departments/people/439/michael-c-milone>

¹¹ <https://www.linkedin.com/in/michael-milone-5a251736/>

¹² <http://pathology.med.upenn.edu/departments/people/439/michael-c-milone>

¹³ <https://www.linkedin.com/in/michael-milone-5a251736/>

¹⁴ <https://www.linkedin.com/in/bruce-levine-9976859/>

¹⁵ <http://pathology.med.upenn.edu/departments/people/291/bruce-l-levine>

David L. Porter

David L. Porter is the Jodi Fisher Horowitz Professor in Leukemia Care Excellence, and Director of Blood and Marrow Transplantation at the Hospital of the University of Pennsylvania.¹⁶ He was with the University at least as early as 2002 when working in the division of Hematology-Oncology.¹⁷ Dr. Porter, as well as Dr. Milone, are also the two clinical collaborators in the Nanomedicine Center for Mechanobiology Directing the Immune Response, which receives funding from the NIH Common Fund.¹⁸

The NIH RePORTER website shows that the 2014 Patents share an identical “Core NIH Project Number” for NIH grant number R01CA105216

The NIH RePORTER website is a tool that “allows users to search a repository of NIH funded research projects”.¹⁹ NIH grant number R01CA105216, entitled “Culture Systems to propagate [sic] Human T cell Subsets” and given to Dr. Carl H. June at the University of Pennsylvania, is connected to 12 patents (see Figure 1). This project was awarded a total of \$1,460,542 from 2004 to 2008 to study antigen presenting cells and T cell subsets for cancer and HIV immunotherapy.

The findings from this project were published in 31 articles found in academic peer-reviewed journals. These findings are related to and support claims from patents listed in Table 2, including 8916381, 8975071, 9102760, 9101584 and 9102761. For example, Dr. June’s lab reported on better ways to culture and grow CAR T cells, and, characterized CARs constructed with multiple intracellular co-stimulatory domains such as CD28 or 4-1BB with CD3zeta.²⁰ These signaling domains are claimed as key parts of the CAR construction in the 2014 patents.

Methods and compositions in the 2014 patents clearly stem from project R01CA105216 and other NIH funded research conducted in Dr. June’s laboratory. Though the NIH reports these patents to be connected to R01CA105216, there is a failure to mention the government interests within the patents.

Figure 1: Screenshot of NIH-RePORTER Results (taken October 10, 2017) of Patents Connected to Grant Number R01CA105216.

¹⁶ <https://www.med.upenn.edu/apps/faculty/index.php/g348/p4492>

¹⁷ https://www.researchgate.net/publication/10953797_Umbilical_cord_blood_transplantation_Where_do_we_stand

¹⁸ <https://commonfund.nih.gov/nanomedicine/devcenters/mechanicalbiology>

¹⁹ <https://projectreporter.nih.gov/reporter.cfm>

²⁰ Frigault MJ *et al.* Identification of chimeric antigen receptors that mediate constitutive or inducible proliferation of T cells. *Cancer Immunol Res.* Apr 2015
(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4390458/#SD1>)

U.S. Department of Health & Human Services

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NIH Project Number	Patent Number	Patent Title	Patent Owner	Primary Agency
R01CA105216	7754482	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	8722400	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	9102791	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	9102760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	8979573	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	8911903	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	9135426	ICCV antibody regulates the expansion and function of interleukin-2 human TH17 cells	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	9572496	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	8916381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	8161594	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01CA105216	9108156	Use of chimeric antigen receptors on human T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	NIH

Table 4 presents the 12 patents in the ReReporter search for NIH grant R01CA105216. The patents with a blue background are the 2014 patents.

Table 4: The ReReporter Designated Patents for Grant R01CA105216

NIH Grant	Patent	Title	Grantee	Federal rights disclosed on patent
R01CA105216	7,754,482	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	R21 AI060477, R01 CA105216 R01 AI 057838
R01CA105216	8,722,400	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	R21 AI060477, R01 CA105216 R01 AI057858
R01CA105216	8,906,682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216,

				RO1AI057838 RO11113482
R01CA105216	8,911,993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838 RO11113482
R01CA105216	8,916,381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	8,975,071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,101,584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,102,760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,102,761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,133,436	ICOS critically regulates the expansion and function of inflammatory human Th17 cells	UNIVERSITY OF PENNSYLVANIA	5R01CA105216, 1R01CA120409, 5P01CA066726 R01A1057838
R01CA105216	9,328,156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838 RO11113482
R01CA105216	9,572,836	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, 1PN2-EY016586, 1R01CA105216, 1R01CA120409, RO1AI057838, R01113482

The NIH RePORTER website shows that the 2014 Patents share an identical "Core NIH Project Number" for NIH grant number R01AI057838

Chimeric antigen receptors are composed of different segments having distinct functions in antigen recognition, signaling and co-stimulation. Understanding the right combination of these segments is important in the function of the CAR and, the activation and survival of the T cell. T cell activation enables these to multiply and allows for the cells to respond to tumors they recognize. The NIH funded project R01AI057838 entitled "Regulation of Human T Cell Activation by the CD28 Family" aims to discern the mechanism behind antigen-dependent signaling pathways responsible for survival and anti-tumor functions so that clinicians can better control therapeutic T cells. Specifically this project studies signaling and activation through

CD28 and ICOS. The R01AI057838 grant is connected to 12 patents including the 2014 patents. Embodiments of second generation CARs described in the 2014 patents incorporate co-stimulatory fragments, such as CD28 and ICOS, into their intracellular domains. Additionally, published results relevant to the 2014 patents appear in articles supported by the R01AI057838 grant. Scientific articles of particular interest are; "Chimeric receptors containing CD137 signal transduction domains mediate enhanced survival of T cells and increased antileukemic efficacy in vivo", "The inducible costimulator (ICOS) is critical for the development of human T(H)17 cells" and "CD28 costimulation is essential for human T regulatory expansion and function".^{21, 22, 23} The R01AI057838 project grant was awarded to Dr. James L Riley at University of Pennsylvania, from 2004 to 2008. The total amount of funding for these four years was \$1,731,361.²⁴

Figure 2: Screenshot of NIH-RePORTER Results (taken October 11, 2017) of Patents Connected to Grant Number R01AI057838.

Search Results

ABOUT RePORTER RESULTS

There were 12 connections of patents to projects matching your search criteria. Click on the column header to sort the results.

Grant/PI Project Number	Patent Number	Patent Title	Patent Owner	Primary Agency
R01AI057838	7754482	Artificial antigen presenting cells and uses thereof	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8722466	Artificial antigen presenting cells and uses thereof	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8875071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9102781	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8911893	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9102790	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8133438	ICOS critically regulates the expansion and function of effector human TH17 cells	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9572636	Methods for increasing the survival of transgenic T cells for gene delivery	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8918381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9101594	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8978158	Use of chimeric antigen receptor modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	NIH

²¹ Milone MC et al. Chimeric receptors containing CD137 signal transduction domains mediate enhanced survival of T cells and increased antileukemic efficacy in vivo. Mol Ther. Aug 2009

²² Paulos CM et al. The inducible costimulator (ICOS) is critical for the development of human T(H)17 cells. Sci Transl Med. Oct 2010

²³ Golovina TN et al. CD28 costimulation is essential for human T regulatory expansion and function. J Immunol. Aug 2008

²⁴ <https://projectreporter.nih.gov>

We checked the patent disclosures on the twelve patents identified by RePorter as relevant to NIH Grant R01A1057838. As reported in Table 5, all disclosed federal funding except for the five “2014” patents.

Table 5: The 12 RePorter-Designated Patents for Grant R01A1057838

NIH Grant	Patent	Title	Grantee	Federal rights disclosed on patent
R01A1057838	9,572,836	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, 1PN2-EY016586, 1R01CA105216, 1R01CA120409, RO1A1057838, RO1113482,
R01A1057838	9,328,156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1A1057838, RO1113482
R01A1057838	9,133,436	ICOS critically regulates the expansion and function of inflammatory human Th17 cells	UNIVERSITY OF PENNSYLVANIA	5R01CA105216, 1R01CA120409, 5P01CA066726, R01A1057838
R01A1057838	9,102,761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01A1057838	9,102,760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01A1057838	9,101,584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01A1057838	8,975,071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01A1057838	8,916,381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01A1057838	8,911,993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1A1057838, RO1113482
R01A1057838	8,906,682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1A1057838, RO1113482
R01A1057838	8,722,400	Artificial antigen presenting cells and	UNIVERSITY OF	R21 AI060477,

		uses therefor	PENNSYLVANIA	R01 CA105216, R01 AI057858.
R01AI057838	7,754,482	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	R21 AI060477, R01 CA105216, R01 AI 057838

The NIH RePORTER website shows that the 2014 Patents share an identical “Core NIH Project Number” for NIH grant number K24CA117879

Nine patents, including the 2014 patents, are affiliated with the K24CA117879 “Mid-career Investigator Award in Allogeneic Adoptive Immunotherapy” project (Figure 3). Dr. David Porter, from the University of Pennsylvania, was awarded \$777,980 between 2006 and 2010, to conduct research under this project. K42 mid-career grants are awarded to clinicians for “patient-oriented research”.²⁵ The research conducted under this grant applied to cellular immunotherapy against cancer. Importantly, grant K24CA117879 supported the crucial but small 2011 UPenn clinical study with Dr. June, “Chimeric Antigen Receptor–Modified T Cells in Chronic Lymphoid Leukemia” (NCT01029366) that demonstrated the potential of their CAR T cell therapy in leukemia. Shortly after this study, Novartis gave UPenn funding towards a research center in exchange for exclusive worldwide rights to CARs developed at UPenn.²⁶

Figure 3: Screenshot of NIH-RePORTER Results (taken October 11, 2017) of Patents Connected to Grant Number K24CA117879.

Search Results				
ABOUT REPORTER RESULTS				
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There were 9 connections of patents to projects matching your search criteria. Click on the column header to sort the results.				
Core NIH Project Number	Patent Number	Patent Title	Patent Owner	Primary Agency
K24CA117879	8811933	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8975071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	9102760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	9102761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	9572830	Methods for assessing the suitability of transduced T cells for gene therapy	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	9161564	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8916581	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8328156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	NIH

²⁵ https://grants.nih.gov/grants/funding/funding_program.htm

²⁶ <https://www.elsevier.com/connect/penn-and-novartis-collaborate-on-new-cancer-drug>

We checked the patent disclosures on the nine patents identified by RePorter as relevant to NIH Grant **K24CA117879**. As reported in Table 6, all disclosed federal funding exception for the five “2014” patents.

Table 6: The 9 RePorter Designated Patents for Grant K24CA117879.

NIH Grant	Patent	Title	Grantee	Federal rights disclosed on patent
K24CA117879	9572836	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, 1PN2-EY016586, 1R01CA105216, 1R01CA120409, RO1AI057838, RO1113482
K24CA117879	9328156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, RO1113482
K24CA117879	9102761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	9102760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	9101584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	8975071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	8916381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	8911993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, RO1113482
K24CA117879	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, RO1113482

III. In the Case of a Failure to Disclose, the Government May Reclaim the Invention

Failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the Federal Government to “receive title to any subject invention not disclosed to it within such time” (emphasis added).

In the past, the federal government has utilized its authority to claim title in subject inventions that have not been properly disclosed, as in the case of *Campbell Plastics Engineering & Mfg., Inc. v. Brownlee*, 389 F.3d 1243 (Fed. Cir. 2004) (finding that federal government claim of title in invention was legitimate under federal acquisition regulations and supported by the Bayh-Dole Act where disclosure submissions were “piecemeal” and violated the contractual agreement with the government); see also *Central Admixture Pharmacy Services, Inc. v. Advanced Cardiac Solutions, P.C.*, 482 F.3d 1347, 1352-53 (Fed. Cir. 2007) (“Critically, *Campbell Plastics* holds that a Bayh–Dole violation grants the government *discretionary* authority to take title. . . . When a violation occurs, the government can choose to take action; thus, title to the patent may be voidable.”).

In *Campbell Plastics*, the court found that the contract was clear and unambiguous, but moreover the government’s claim to title was “buttressed by the policy considerations behind the Bayh-Dole Act.” *Id.* at 1248. These include, specifically under 35 U.S.C. § 200, the need “to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions.”

IV. Conclusion

We believe that there is sufficient evidence to warrant an investigation into this matter. If the 2014 patents are subject inventions under the Bayh-Dole Act, UPenn has an affirmative obligation to disclose the inventions to the government and to explicitly state the government’s rights in the patents. The 2014 patents appear to have failed to do so in spite of the abundant evidence suggesting that they are subject inventions.

The failure to disclose government rights in a subject invention does a disservice to taxpayers, consumers and patients.

We request a meeting at your earliest convenience to discuss this matter in further detail.

Sincerely,



James Love
Director
Knowledge Ecology International
james.love@keionline.org



Andrew S. Goldman, Esq.
Counsel, Policy and Legal Affairs
andrew.goldman@keionline.org



Diane Singhroy
Scientific and Technical Advisor
diane.singhroy@keionline.org

Cc:

Gary M. Beck, Advisor for External Affairs, HHS
Ann Hammersla, Director of OPERA's Division of Extramural Inventions and Technology
Resources, NIH

Dear Acting Secretary Hargan:

Attached please find a letter from Knowledge Ecology International requesting that you initiate an investigation into the failure of the Trustees of the University of Pennsylvania to disclose the NIH interest in five particular patents relating to chimeric antigen receptor T Cell (CAR T) therapy.

The Bayh Dole Act and related regulations require that contractors disclose subject inventions to the funding federal agency and place certain language in patent applications (and patents issuing thereon) statements specifying the role that federal funds played in the development and acknowledging that the Government retains certain rights in the invention. The attached letter provides substantial evidence suggesting the Trustees have failed to abide by these legal requirements, and discusses the public's interest in disclosure particularly in the context of CAR T, as well as certain remedies available to the government for nondisclosure including reclamation of the invention.

We would appreciate the opportunity to discuss this matter in further detail with your office.

Sincerely,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org<<mailto:andrew.goldman@keionline.org>> // www.twitter.com/ASG_KEI<http://www.twitter.com/ASG_KEI>

tel.: +1.202.332.2670

www.keionline.org<<http://www.keionline.org>>

Dear Acting Secretary Hargan:

Attached please find a letter from Knowledge Ecology International requesting that you initiate an investigation into the failure of the Trustees of the University of Pennsylvania to disclose the NIH interest in five particular patents relating to chimeric antigen receptor T Cell (CAR T) therapy.

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We would appreciate the opportunity to discuss this matter in further detail with your office.

Sincerely,

Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

FW: Request to Investigate U Penn Failure to Disclose Federal Funding of CAR T Patents

Oct 16 letter attached.

From: Andrew S. Goldman [mailto:andrew.goldman@keionline.org]

Sent: Wednesday, October 18, 2017 12:36 PM

To: Hargan, Eric (OS/IOS)

Cc: Beck, Gary (OS/IEA); Hammersla, Ann (NIH/OD) [E]; Jamie Love; Diane Singhroy

Subject: Re: Request to Investigate U Penn Failure to Disclose Federal Funding of CAR T Patents

Dear all:

With regard to the letter we sent on Oct 16 regarding nondisclosure of government rights in certain CAR T patents, we received a statement from the University of Pennsylvania that they did disclose NIH funding via iEdison and in the patents. We found that UPenn did file certificates of correction for the five patents in question, but these certificates were only viewable in the USPTO database as image files, and not in the searchable text.

We will be following up with UPenn on this matter, and intend to ask USPTO and NIH to improve the manner in which government rights in patents, including via corrections, are disclosed to the public.

The full text of our statement with regard to these certificates of correction is available here:
<http://www.keionline.org/node/2882>

Sincerely,

REL0000024155.0004

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org<<mailto:andrew.goldman@keionline.org>> //

www.twitter.com/ASG_KEI<http://www.twitter.com/ASG_KEI>

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www.keionline.org<<http://www.keionline.org>>

On Mon, Oct 16, 2017 at 5:02 PM, Andrew S. Goldman

<andrew.goldman@keionline.org<<mailto:andrew.goldman@keionline.org>>> wrote:

Dear Acting Secretary Hargan:

Attached please find a letter from Knowledge Ecology International requesting that you initiate an investigation into the failure of the Trustees of the University of Pennsylvania to disclose the NIH interest in five particular patents relating to chimeric antigen receptor T Cell (CAR T) therapy.

The Bayh Dole Act and related regulations require that contractors disclose subject inventions to the funding federal agency and place certain language in patent applications (and patents issuing thereon) statements specifying the role that federal funds played in the development and acknowledging that the Government retains certain rights in the invention. The attached letter provides substantial evidence suggesting the Trustees have failed to abide by these legal requirements, and discusses the public's interest in disclosure particularly in the context of CAR T, as well as certain remedies available to the government for nondisclosure including reclamation of the invention.

We would appreciate the opportunity to discuss this matter in further detail with your office.

Sincerely,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

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From: Andrew S. Goldman [andrew.goldman@keionline.org]
Sent: 10/16/2017 9:02:34 PM
To: Hargan, Eric (OS/IOS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=690e5e2246a84c9ba4641e65306f8885-Eric.Hargan]
CC: Beck, Gary (OS/IEA) [Gary.Beck@hhs.gov]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]; Jamie Love [james.love@keionline.org]; Diane Singhroy [diane.singhroy@keionline.org]
Subject: Request to Investigate U Penn Failure to Disclose Federal Funding of CAR T Patents
Attachments: HHS, Penn CAR T patent disclosures 17 Oct 2017, final.pdf

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